

**ABSTRACT BOOK**



# **4<sup>th</sup> Balkan Congress of Nuclear Medicine**

**Ohrid 2015**



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### **WITH CONTRIBUTION**

European Association of Nuclear Medicine & European School of Nuclear Medicine  
Institute of Pathophysiology and Nuclear Medicine Academic Isak S Tadzer,  
Medical Faculty, University Ss Cyril and Methodius, Skopje  
Ministry of Health, Of Republic of Macedonia  
Institut Francais, Skopje  
World Association for Radionuclide Molecular Therapy

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**Clinical applications of 18F-fluorocholine: current status and potential future applications**

**JN TALBOT**

**Médecine Nucléaire, Hôpital Tenon,**

**AP-HP & Université Pierre et Marie Curie, Paris**

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**Medical University - Plovdiv**

**Medical Imaging Department**

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**Roberto Delgado-Bolton<sup>1</sup> and Adriana K. Calapaquí-Terán<sup>2</sup>**

**<sup>1</sup>Logroño, La Rioja**

**<sup>2</sup>Madrid**

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**National Oncology University Hospital Center-SHATO, Clinic of Nuclear Medicine, Sofia**

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**Dept of Nuclear Medicine**

**Central University Emergency Military Hospital, Bucharest**

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- 1. Centre de Médecine Nucléaire, Institute Andrée Dutreix, Centre de Cancérologie et Radiothérapie Nord Littoral, Dunkerque**
- 2. Department of Nuclear Medicine, « Colentina » Clinical University Hospital, Bucharest**

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**<sup>1</sup>Department of Nuclear Medicine, Clinical Center Kragujevac and Faculty of Medical Sciences, University of Kragujevac**

**<sup>2</sup>Polytechnic School in Cacak, University of Kragujevac**

**<sup>3</sup>Prizma Company, Kragujevac, <sup>4</sup>Department of Nuclear Medicine, Clinical Center Nis and Medical Faculty University of Nis**

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**S.Sergieva**

**Department of Nuclear Medicine, Sofia Cancer Center**

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**Read the small letters of the Guidelines for ablation therapy and apply them to the patients. Size does not always matters.**

**SavvasFrangos MD, FEBNM, Nuclear Medicine Specialist**

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**Ajdinovic B**

**Military Academy, Belgrade**

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**<sup>1</sup>Institute of Nuclear Medicine, <sup>2</sup>Clinic for Plastic and Reconstructive Surgery, <sup>3</sup>Clinic for Dermatology, <sup>4</sup>Center of Pathology and Forensic Medicine**

**Military Medical Academy, Belgrade**

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**Department of Nuclear Medicine, Sofia Cancer Center, Sofia**

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**Prof. Dr. Ömer Uğur**

**Hacettepe University**

**Ankara**

**[ougur@hacettepe.edu.tr](mailto:ougur@hacettepe.edu.tr)**

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**Miladinova D. MD PhD, Stefanova M. MD MSc**

**Institute of Pathophysiology and Nuclear Medicine Acad.Isak S.Tadzer, Faculty of medicine, University SsCyril and Methodius, Skopje**

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**Venjamin Majstorov**

**Institute of Pathophysiology and Nuclear Medicine, Medical Faculty, University Ss' Cyril and Methodius, Skopje**

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**<sup>1</sup>Faculty of Medical Sciences, "GoceDelcev" University, Stip**

**<sup>2</sup>European Institute of Oncology, Milan**

**<sup>3</sup>Faculty of Natural Sciences and Mathematics, University "Ss. Cyril and Methodius" Skopje**

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**Faculty of Medical Sciences, Goce Delcev University Stip**

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**<sup>1</sup>Department of Pharmacy, Faculty of Medical Sciences, University Goce Delčev – Štip**

**<sup>2</sup>Department of Chemistry, Faculty of Natural Sciences and Mathematics, University “Ss. Cyril and Methodius” – Skopje**

**<sup>3</sup>Department of Chemical and Pharmaceutical Sciences, University of Ferrara, Ferrara**

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**Riemer H..A. Slart, MD, PhD**

**Nuclear Medicine Physician, staff member of the department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen**

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**Department of nuclear medicine,**

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**Department for Nuclear Medicine,**

**University Medical Centre Ljubljana**

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**S. Rep, L. Ležaić**

**Department for Nuclear Medicine,**

**University Medical Centre Ljubljana,**

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**Jovanovska A, Dimcheva M, Sergieva S**

**Department of Nuclear Medicine, Sofia Cancer Center, Sofia**

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**Ugrinska A**

**University "Ss Cyril and Methodius", Medical Faculty, Institute of Pathophysiology and Nuclear Medicine "A. Isak S Tadzer", Skopje**

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**John T. Koutsikos, MD, PhD**

**Nuclear Medicine physician, Nuclear Medicine Dept.**

**401 General Military Hospital, Athens**

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**Zehra Ozcan, MD, FEBNM,**

**Ege University School of Medicine**

**Department of Nuclear Medicine**

**35100 Bornova, Izmir**

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- 1. University of Belgrade, Faculty of Medicine, Center for Nuclear Medicine, Clinical Center of Serbia**
- 2. University of Belgrade, Faculty of Electrical Engineering**
- 3. Center for Nuclear Medicine, Clinical Center of Serbia Belgrade**

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- 1. University of Belgrade, Faculty of Medicine, Center for Nuclear Medicine, Clinical Center of Serbia**
- 2. University of Belgrade, Faculty of Electrical Engineering**
- 3. Military Medical Academy, Belgrade**

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<sup>1</sup>Department for Nuclear Medicine, University Medical Centre Ljubljana

<sup>2</sup>Department of Endocrinology, Diabetes and Metabolic Diseases, University Medical Centre Ljubljana

<sup>3</sup>Department for Abdominal Surgery, University Medical Centre Ljubljana

<sup>4</sup>Nuclear Medicine Unit, Department of Endocrinology, Jagiellonian University Medical School, Cracow <sup>5</sup>National Centre for Nuclear Research Radioisotope Centre POLATOM, Otwock

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<sup>1</sup>University of Belgrade - Faculty of Electrical Engineering, <sup>2</sup>National Cancer Research Center, <sup>3</sup>Center for Nuclear Medicine, Clinical Center of Serbia, <sup>4</sup>University of Belgrade - Faculty of Medicine, Belgrade

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Koljevic Markovic<sup>1</sup>, M. Jankovic, G. PupiĆ R. Džodić<sup>1</sup> National Cancer Research Center, Belgrade, <sup>2</sup>Faculty of Electrical Engineering, University of Belgrade, Belgrade, <sup>3</sup>Faculty of Medicine, University of Belgrade

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L. Brajković<sup>1</sup>, D. Sokić<sup>2</sup>, N. Vojvodić<sup>2</sup>, A. Ristić<sup>2</sup>, S. Janković<sup>2</sup>, D. Šobić-Šaranović<sup>1</sup>, V. Artiko<sup>1</sup>

Center for Nuclear Medicine<sup>1</sup>, Clinical Center of Serbia

Clinic for Neurology<sup>2</sup>, Clinical Center of Serbia, Belgrade, Serbia

lelabrajko62@gmail.com

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## POSTER PRESENTATION

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Pawlak D, Wojdowska W, Parus J, Cieszykowska I, Janiak T, Jerzyk K, Mielcarski M, Barcikowski T, Garnuszek P, Mikołajczak R. National Centre for Nuclear Research, Radioisotope Centre POLATOM, Otwock

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Ince S, Alagoz E, Emer O, San H, Okuyucu O, Ayan A, Karacalioglu O, Gunalp B, Arslan N. Gulhane Military Medical Academy and School of Medicine, Department of Nuclear Medicine, Etlik, Ankara

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T.Tripunoski<sup>1</sup> and D.Mathe,<sup>2</sup> L.Balogh,<sup>2</sup> A.Polyak,<sup>2</sup> A. Ugrinska<sup>1</sup>, Gy. A. Janoki,<sup>2</sup> S. Stojanovski<sup>1</sup>, D. Miladinova<sup>1</sup>, E. Janevik-Ivanovska<sup>3</sup>, O.Vaskova<sup>1</sup>

<sup>1</sup>Institute of Pathophysiology and Nuclear Medicine, Medical Faculty, Skopje

<sup>2</sup>Frederic Joliot-Curie National Institute of Radiobiology and Radiohygiene, Dept. of Applied Radioisotopes, Budapest

<sup>3</sup>Faculty of Medical Sciences, Goce Delcev University, Stip

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### Comparative characteristics of radionuclides Tcm99MIBI and Tcm99TETROFOSMIN in process of biodistribution

Mihajlova S, Risteski Lj, Mihajlova S, Sirvini Z, Sekulovska M  
Department of nuclear medicine, Clinical hospital -Bitola

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<sup>1</sup>Nuclear Medicine Department Hygeia SA, Athens, Marousi, <sup>2</sup>Medical Physics Department, Hygeia S.A., Athens, Marousi

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Bojic L<sup>1</sup>, Sobic – Saranovic D<sup>2</sup>, Petrasinovic Z<sup>3</sup>, Djordjevic Dikic A<sup>3</sup>, Artiko V<sup>2</sup>, Obradovic V<sup>2</sup>

<sup>1</sup>Department of nuclear medicine, Clinical Centre of Montenegro, Podgorica, <sup>2</sup>Center of nuclear medicine, Clinical Centre of Serbia, Belgrade <sup>3</sup>Clinic for Cardiology, Clinical Center of Serbia, Belgrade

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**1. Department of Nuclear medicine, Clinical center University of Sarajevo**

**2. Heart center, Clinical center University of Sarajevo**

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**SHSKUK, Clinic for nuclear medicine, Prishtinë**

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**Institute of Pathophysiology and Nuclear Medicine<sup>1</sup>, Clinic of Endocrinology and metabolism disease<sup>2</sup>, Medical Faculty, UKIM, Skopje**

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#### **ROLE OF FDG-PET IN RENAL CANCER**

**Nikaki A<sup>1</sup>, Kechagias D<sup>1</sup>, Vlachou F<sup>1</sup>, Filippi V<sup>1</sup>, Pipikos T<sup>1</sup>, Savvidou D<sup>1</sup>, Razi E<sup>2</sup>, Gogos K<sup>3</sup>, Merisoglou S<sup>1</sup>, Andreou I<sup>1</sup>, Efthymiadou R<sup>1</sup>, Prassopoulos V<sup>1</sup>;**

**<sup>1</sup>PET/CT Department ,Hygeia S.A., Athens, Marousi, <sup>2</sup>3rd Oncology Department, Hygeia S.A., Athens, Marousi, <sup>3</sup>Medical Physics Department ,Hygeia S.A., Athens, Marousi**

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#### **FDG-PET/CT IN SOLITARY PULMONARY NODULE (SPN) ASSESSMENT**

**Vlachou F<sup>1</sup>, Filippi V<sup>1</sup>, Nikaki A<sup>1</sup>, Savvidou D<sup>1</sup>, Kosmidis P<sup>2</sup>, Iliadis K<sup>3</sup>, Pipikos T<sup>1</sup>, Gogos K<sup>4</sup>, Dalianis K<sup>4</sup>, Andreou I<sup>1</sup>, Efthymiadou R<sup>1</sup>, Prassopoulos V<sup>1</sup>**

**<sup>1</sup>PET/CT Department ,Hygeia S.A., Athens, Marousi, <sup>2</sup>2nd Internal Medicine - Oncology Clinic Hygeia SA, Athens, Marousi, <sup>3</sup>Thoracic Surgery Clinic Hygeia SA, Athens, Marousi, <sup>4</sup>Medical Physics Department ,**

**Hygeia S.A., Athens, Marousi**

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**Sarcoidosis and 18F-FDG PET/CT imaging - don't miss malignancy**

**Grmek M<sup>\*</sup>, Koren Pucelj N<sup>\*\*</sup>, Tercelj M<sup>\*\*</sup>**

**University Medical Centre Ljubljana, <sup>\*</sup>Dept. for Nuclear Medicine, <sup>\*\*</sup>Clinical Dept. for Pulmonary Diseases and Allergy, Ljubljana**

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**A.TODOROV, L. CHERVENKOV, V.SIRAKOV, M. STOEVA, K. VELKOVA**

**Medical University - Plovdiv**

**Medical Imaging Department**

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## **INFLUENCE OF NATURAL RADIOACTIVITY OF LUTETIUM IN THE PET DEVICES WITH LSO SCINTILLATORS**

**Antic V.<sup>1,2</sup>, Stankovic K.<sup>2</sup>**

<sup>1</sup>Center for Nuclear Medicine, University Clinical Centre of Serbia, Belgrade, Serbia, Pasterova 2, 11000 Belgrade

<sup>2</sup> School of Electrical Engineering, University of Belgrade, Bulevar kralja Aleksandra 73, 11120 Belgrade

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**Beatović S<sup>1</sup>, Jakšić E<sup>1</sup>, Janković M<sup>2</sup>, Antić V<sup>3</sup>, Šobić-Šaranović D<sup>1</sup>, Artiko V<sup>1</sup>.**

1. University of Belgrade, Faculty of Medicine, Center for Nuclear Medicine, Clinical Center of Serbia
2. University of Belgrade, Faculty of Electrical Engineering
3. Center for Nuclear Medicine, Clinical Center of Serbia  
Belgrade

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## **ADVANCED QUANTITATIVE ANALYSIS OF DYNAMIC RENAL SCINTIGRAPHY: ROLE OF PHYSIOLOGIC PARAMETERS OF KIDNEY OUTPUT IN THE DIAGNOSIS OF UPPER URINARY TRACT OBSTRUCTION**

**Beatović S<sup>1</sup>, Jakšić E<sup>1</sup>, Janković M<sup>2</sup>, Radulović M<sup>3</sup>, Šobić-Šaranović D<sup>1</sup>, Artiko V<sup>1</sup>**

1. University of Belgrade, Faculty of Medicine, Center for Nuclear Medicine, Clinical Center of Serbia
2. University of Belgrade, Faculty of Electrical Engineering
3. Military Medical Academy, Belgrade

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## **Whole body and finger effective dose for medical workers operating in a PET/CT department with statistical analysis**

**Dalianis K<sup>1</sup>, Kollias G<sup>1</sup>, Vlachou F<sup>2</sup>, Filippi V<sup>2</sup>, Andreou J<sup>2</sup>, Efthymiadou R<sup>2</sup>, Prassopoulos V<sup>2</sup>**

<sup>1</sup>Medical Physics Department, Hygeia S.A., Athens, Marousi, <sup>2</sup>PET/CT Department, Hygeia S.A., Athens, Marousi

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## **OCCUPATIONAL EXPOSURE IN PET/CT DIAGNOSTICS: WHOLE BODY AND EXTREMITY DOSES**

**Antic V.<sup>1,2</sup>, Ciraj-Bjelac O.<sup>2,3</sup>, Stankovic J.<sup>2,3</sup>, Arandjic D.<sup>2,3</sup>, Bozovic P.<sup>2,3</sup>**

<sup>1</sup>Center for Nuclear Medicine, University Clinical Centre of Serbia, Belgrade, Serbia, Pasterova 2, 11000 Belgrade

<sup>2</sup>School of Electrical Engineering, University of Belgrade, Bulevar kralja Aleksandra 73, 11120 Belgrade

<sup>3</sup>Vinča Institute of Nuclear Sciences, University of Belgrade, Mike Petrovica Alasa 12-14, 11001 Belgrade

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**Apostolova Paulina, Sterjova Marija, Smilkov Katarina, Gorgieva Ackova Darinka, Delipetrev Katarina, Janevik Ivanovska Emilija**

Faculty of Medical Sciences, University Goce Delčev – Štip

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## **ESTABLISHMENT OF PRODUCTION LABORATORY FOR FLUORODEOXYGLUCOSE 18F (18F-FDG)**

**Marija Atanasova, Maja Jancovska, Katerina Kolevska, Maja Velickovska, Filip Jolevski, Emilija Janevik-Ivanovska**

Faculty of Medical Sciences, Unit for PET implementation, University Goce Delčev – Štip

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## **QUALITY CONTROL OF PET RADIOPHARMACEUTICALS, AN IMPERATIVE FOR SUCCESSFUL CLINICAL OUTCOMES**

**Maja Velickovska, Filip Jolevski, Marija Atanasova, Maja Jancovska, Katerina Kolevska, Emilija Janevik-Ivanovska**

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**Joel Munene Muchira<sup>1,3</sup>, David Mwanza Wanjeh<sup>1,3</sup>, Aschalew Alemu<sup>2,3</sup>, Emilija Janevik-Ivanovska**

<sup>1</sup>Ministry of Health, Kenya

<sup>2</sup>Faculty of Medicine, Addis Ababa

<sup>3</sup>Faculty of Medical Sciences, Goce Delcev University, Shtip

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**Petrov T<sup>1</sup>, Garcheva M<sup>1</sup>, Elenkova A<sup>2</sup>, Vasilev V<sup>2</sup>, Ivanova R<sup>2</sup>, Zacharieva S<sup>2</sup>, Kostadinova I<sup>1</sup>**

**<sup>1</sup>Clinic of nuclear medicine, Medical University, Sofia; <sup>2</sup>Clinical center of endocrinology, Medical University, Sofia**

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**<sup>1</sup>Institute of Pathophysiology and Nuclear Medicine, Medical Faculty, Skopje**

**<sup>2</sup>Psychiatric Hospital, Psychogeriatric Center – Skopje**

**<sup>3</sup>Institute of Epidemiology and Biostatistics, Medical Faculty, Skopje**

**<sup>4</sup>Institute for Ageing and Health, Newcastle University**

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**L. Brajković<sup>1</sup>, V. Kostić<sup>2</sup>, M. Svetel<sup>2</sup>, E. Stefanova<sup>2</sup>, I. Petrović<sup>2</sup>, M. Jecmenica-Lukić<sup>2</sup>,**

**D. Šobić-Šaranović<sup>1</sup>, V. Artiko<sup>1</sup>**

**Center for Nuclear Medicine<sup>1</sup>, Clinical Center of Serbia,**

**Clinic for Neurology<sup>2</sup>, Clinical Center of Serbia, Belgrade**

**lelabrajko62@gmail.com**

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**Nikaki A<sup>1</sup>, Savvidou D<sup>1</sup>, Prassopoulos V<sup>1</sup>, Filippi V<sup>1</sup>, Tsougos I<sup>2</sup>, Vlachou F<sup>1</sup>, Andreou I<sup>1</sup>, Pipikos T<sup>1</sup>, Dalianis K<sup>3</sup>, Papoutsis V<sup>1</sup>, Efthymiadou R<sup>1</sup>, Georgoulas P<sup>4</sup>;**

**<sup>1</sup>PET/CT Department ,Hygeia S.A., Athens, Marousi, <sup>2</sup>Medical Physics Department**

**,University of Thessaly, Larissa, <sup>3</sup>Medical Physics Department ,Hygeia S.A., Athens,**

**Marousi, <sup>4</sup>Nuclear Medicine Department,**

**University of Thessaly, Larissa**

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**Kostadinova I<sup>1</sup>, Minkin K<sup>2</sup>, Dimova P<sup>2</sup>, Zlatareva D<sup>3</sup>, Hadjiiska V<sup>1</sup>**

**<sup>1</sup> Department of Nuclear Medicine, <sup>2</sup> Department of Neurosurgery, <sup>3</sup> Department of Radiology, Medical University, Sofia**

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**Kemerburgaz University, School of Medicine, Nuclear Medicine<sup>1</sup>, Medical Oncology<sup>2</sup>, Istanbul**

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**<sup>1</sup>Nuclear Medicine Department Hygeia SA, Athens, Marousi,<sup>2</sup>Medical Physics Department ,Hygeia S.A., Athens, Marousi <sup>3</sup>CT- MRI Department Hygeia SA, Athens, Marousi**

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**Nuclear Medicine Department Hygeia SA,**

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**<sup>1</sup>Institute of Pathophysiology and Nuclear Medicine, <sup>2</sup>University Clinic for Digestive Surgery, <sup>3</sup>University Clinic for Gastroenterohepatology, <sup>4</sup>Institute of Pathology, Faculty of Medicine, University SsCyril and Methodius, Skopje**

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**<sup>1</sup>University Clinic for Digestive Surgery, <sup>2</sup>Institute of Pathophysiology and Nuclear Medicine, <sup>3</sup>Institute of Pathology, Faculty of Medicine, <sup>4</sup>University Clinic for Gastroenterohepatology Faculty of medicine University SsCyril and Methodius, Skopje**

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**<sup>1</sup>Clinical Hospital Acibadem-Sistina Skopje**

**<sup>2</sup>Institute of Pathophysiology and Nuclear Medicine, Medical Faculty Skopje**

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**Authors: Stojanoski Sinisa 1, Trencev Viktor 2, Angjeleska Meri 1, Ristevska Nevena 1, Pop Gjorceva Daniela 1, Miladinova Daniela 1, Majstorov Venjamin 1, Ugrinska Ana 1, Vaskova Olivija1**

**1 Institute of Pathophysiology and Nuclear Medicine, Acad “Isak S. Tadzer”, 2 Clinic for plastic and reconstructive surgery, Medical Faculty, Skopje**

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**<sup>1</sup>University Surgical Clinic “St.Naum Ohridski” Skopje**

**<sup>2</sup>Clínica Girona, Girona**

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1. Dermatology Clinic-University Clinical Center Prishtina  
2. Department of Nuclear Medicine-University Clinical Center Prishtina  
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1. Dermatology Clinic-University Clinical Center Prishtina  
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2 Institute of Pathophysiology and Nuclear Medicine,  
Medical Faculty Skopje

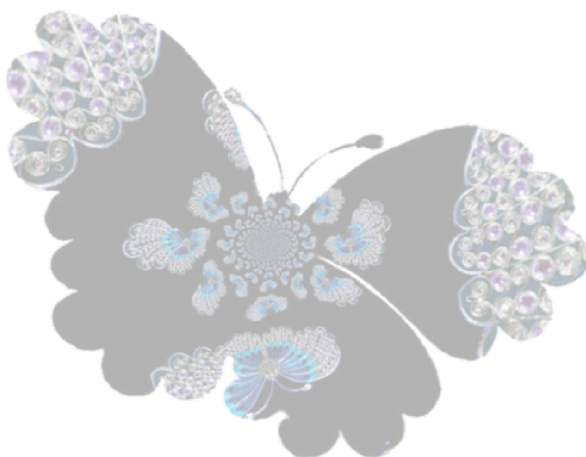
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University Clinic of Radiotherapy and Oncology, Medical Faculty, UKIM, Skopje<sup>1</sup>  
Institute of Pathophysiology and Nuclear Medicine "A. Isak S Tadzer", Medical Faculty, UKIM, Skopje<sup>2</sup>  
Department of Biology, Faculty of Natural Science,  
University of Elbasan, Elbasan<sup>3</sup>

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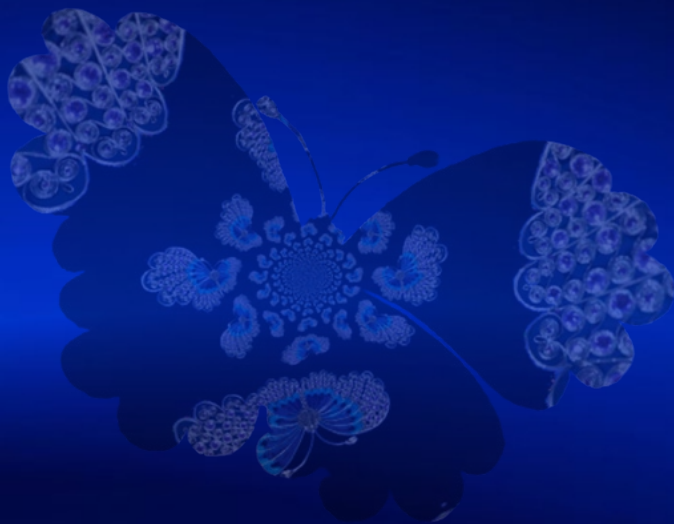
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# INVITED LECTURES

## **Clinical applications of 18F-fluorocholine: current status and potential future applications**

**JN TALBOT**

**Médecine Nucléaire, Hôpital Tenon, AP-HP & Université Pierre et Marie Curie, Paris**

18F-fluorocholine (FCH) has been approved as a clinical PET tracer in France in 2010 and then in several EU countries. The registered indication is search for tissues or structures with an enhanced turn-over of choline, with a documented utility to detect bone metastases of prostate cancer, characterise liver nodules as hepatocellular carcinoma, stage and restage known hepatocellular carcinoma. In prostate cancer FCH is used far beyond detection of bone metastases, it can detect local recurrences, lymph node metastases and distant metastases in soft tissue. It is also effective in castration-resistant cancer to early detect cancer progression under chemotherapy or abiraterone or enzalutamide or 223Ra dichloride.

Furthermore, since the very beginning of its clinical development, FCH proved to be an effective cancer-seeking metabolic tracer, being also taken-up by breast cancer, brain tumours, lung cancer, head and neck cancers, lymphoma ... When compared with FDG, it has several advantages: it can detect neoplasia of low aggressiveness or non-enhanced glucose metabolism (e.g. prostate cancer, well differentiated hepatocellular carcinoma, bronchoalveolar lung cancer ...), it can detect brain metastases or cancer lesions close to the brain (skull, base of the skull), the cancer uptake is generally rapid and plateaus after a few minutes, which allows an easier follow-up of tumour uptake measurement than with FDG with which the delay from injection to imaging must remain fairly constant for monitoring tumour uptake. Its limitation is the high background in the liver which limits the detection of liver metastases generally appearing photopenic. Finally, the utility of FCH is not limited to cancer imaging; it can be useful in the detection and characterisation of benign tumours such as meningiomas, pituitary adenomas and adenomas or hyperplasia of the parathyroid glands.

In summary, FCH is a useful tool in detecting benign tumours and cancers of low malignancy even though it is still taken up by most aggressive forms of cancer. The clinical settings where it may be overpass FDG are becoming more numerous.

**PET/MR planning and preparing for its arrival-a nuclear medicine perspective**  
**So you want to buy a PET-MR**  
**Prof John Buscombe**  
**Cambridge University Hospitals, Cambridge**

The decision to buy a major piece of equipment needs careful consideration. PET-MR machines offer the opportunity to perform studies that cannot normally be done using each modality on its own. Firstly it is important to decide if the machine will be needed to do sequential or simultaneous PET and MR. This may define the type of machine bought. Then it is important to define if the main usage will be research or clinical. The case for the Cambridge campus was that the machine would concentrate on research for dementia and cancer metastases to the liver. This meant that a hyperpolariser would need to be accommodated within the centre.

Ideally any PET-MR would be built into a new building but in reality they are normally required to fit into an existing structure. We are used to the constraints of a PET-CT centre. Many of the issues are similar in that there needs to be a safe area for storing radiopharmaceuticals. An area is needed for patient injection and waiting, though as PET-MR scans can take up to 90 minutes, fewer patient bays are needed. There needs to be a “hot toilet” for injected patients and possibly a pharmacokinetics laboratory.

MR brings new challenges to the nuclear medicine department. An RF cage is needed. There needs to be a pipe to rapidly quench a helium leak. An MR uses a lot of power when its magnets ramp up. New monitoring equipment which is MR compatible is needed. No steel or iron chairs, trolleys etc. Even a steel tungsten syringe shield can kill in a PET MR room.

Is it worth all this effort? Time will tell .

## **Contribution of PET scan in treatment**

### **Vassilios Prassopoulos**

PET/CT has gained a major role through years in medical imaging of oncologic patients, with applications involving a large field of solid tumors and lymphomas. Its contribution has extended to direct and alter treatment decisions in malignant diseases in  $\approx 30\%$  of patients. PET/CT imaging has been included in guidelines concerning treatment decisions in several occasions: in adult Hodgkin and aggressive non-Hodgkin lymphomas for initial staging and end of chemotherapy and/or radiotherapy evaluation, as well as in pediatric and adolescent Hodgkin lymphomas; in initial staging of non-small-cell lung cancer for mediastinal status determination and exclusion of distant metastasis; in head and neck cancer in M and bilateral nodal involvement where significant treatment decisions are going to be received, in cases of cervical lymphadenopathy of unknown primary site as well as in assessing staging and recurrence for equivocal findings and therapeutic strategies judgments. PET/CT is, also, applied in bone marrow assessment in Hodgkin lymphomas, in cases of colon cancer for metastatic disease estimation when hepatic metastasectomy is considered, in ovarian cancer and particularly in cases of serum cancer indexes raise and cytoreductive surgery selection, in testicular cancer especially for surgery candidates, in melanoma, in prostate cancer, in brain tumors, etc. Finally, one of the most important and widely utilized indications of PET scans in radiation fields planning with impact in tumor volume delineation, atelectasis estimation and additionally in prognosis.

## **KIDNEY ARTERIES ASSESSMENT VIA CT ANGIOGRAPHY**

**A.GEORGIEV, V.SIRAKOV, M. STOEVA, K. VELKOVA**

**Medical University - Plovdiv**

**Medical Imaging Department**

Diagnostic Imaging has a leading role in assessment of the renal stenosis. Renal stenosis discovery frequency has increased recently due to the technical advancements in ultrasound, Doppler imaging, CT angiography (CTA), and Magnetic resonance angiography (MRA). The diagnostic and therapeutic processes are enhanced by various contemporary solutions which also contribute towards understanding of the malignant processes. Diagnostic methods have developed better compared to the therapeutic ones, which is also a tool for better prevention.

The main cause for renal stenosis are arteriosclerotic changes – in approximately 60% of the cases. Fibromuscular dysplasia is a heterogeneous group of idiopathically non-arteriosclerosis segment engagement of the renal artery - the most common with medial hyperplasia. Other causes may be –Takayasu arteriitis, aneurisms, etc.

Renal artery stenosis causes 2 common clinical syndromes – hypertonia and ischemic nephropathy. There are complex relations between renal artery stenosis, arterial hypertonia and renal excretory dysfunction. Lowering the renal perfusion pressure affects not only the renal system, but Na excretion, simpatico tonus, intra-renal prostaglandin concentrating and the production nitroxid. Ischemic neuropathy is a result from renal blood flow obstructions which causes ischemia and excretory malfunction. The cause is not fully studied. Blood flow auto-regulation is not effective when the systolic pressure falls 70/80 mmHg, which may cause reduction of the production of nitrogen oxide, renin-angitensin system activation, local ischemic areas, tubular damage, epitel cells damage and fibrosis. Renal dysfunction is related to the arteriosclerotic renal stenosis.

90 CT renovasographia (RVG) and 200 abdomen and lower extremities CT and DSA angiographies have been conducted in the period 2011 – 2014. An assessment of the kidney arteries and kidney parenchymal saturation have been made following these studies. We have confirmed the role of the ankle brachial index (ABI) as an assessment criteria for the renal artery engagement. Values lower than 0.7 are indicative for screening angiography, while values lower than 0.5 are indicative for renal stenosis.

## **Incorporating PET/CT Imaging in Radiation Oncology Treatment Delivery**

**Roberto Delgado-Bolton<sup>1</sup> and Adriana K. Calapaquí-Terán<sup>2</sup>**

<sup>1</sup>Logroño, La Rioja

<sup>2</sup>Madrid,

The incorporation of functional imaging to Radiation Oncology is one of the important milestones in modern oncology. The metabolic information supplied by PET/CT and PET/MR provides crucial information in oncologic patients for diagnosis, guiding biopsies, initial staging, response monitoring, and recurrent disease detection. Patients referred to Radiation Oncology benefit of these advantages but also of the improved treatment planning and patient management decisions. Taking into account the metabolic information allows more accurate volume delineation and improves response assessment. In the era of personalised medicine PET/CT has a key role as it provides in vivo functional information. This paper will address the role of PET/CT in Radiation Oncology treatment delivery focusing on four important cancers: lung cancer, head and neck cancer, prostate cancer and liver metastatic cancer.

**Lung cancer:** FDG PET/CT is a valuable diagnostic method for non-small cell lung cancer (NSCLC) for staging, therapy assessment, management and prognosis. FDG PET/CT is also a valuable tool in radiation treatment planning and follow-up. In NSCLC, non-operable patients with early stage localised disease are eligible for stereotactic body radiation therapy (SBRT), whereas patients with locally advanced disease are referred to 3D-conventional radiotherapy (3D-CRT). In the early stage patients, PET/CT ensures early stage or localised disease (N0) at the initial diagnosis, it allows better tumour definition, and it helps in a more precise contouring of the GTV. In patients with locally advanced disease PET/CT has a key role at initial diagnosis to ensure the correct stage (N+) and improves treatment planning, allowing a better delimitation of GTV and PTV (guiding the inclusion of PET positive lymph nodes, negative on CT). Following SBRT in patients with stage I NSCLC, the early detection of recurrences is an important issue, especially in patients with mass-like fibrosis. CT and PET characteristics are indicators of local recurrence. Furthermore, a pre-radiotherapy FDG PET/CT may be used to identify the FDG avid volumes which a higher uptake which correlate with post-therapy persistence and may benefit of dose escalation. Another interesting issue is 4D FDG PET/CT based target volume delineation for SBRT of centrally located lung tumours, as it increases the interobserver agreement and may help to avoid geographic misses.



*Head and neck cancer:* Molecular imaging has a key role in head and neck cancer for various indications. As for many other tumour types, FDG PET/CT is by far the most important and most widely applied molecular imaging technique as it is used for identification of unknown primaries, tumour characterisation and prognosis, staging, radiation treatment planning, treatment adaptation, relapse detection and follow-up. For each of these indications, FDG PET/CT has its own strengths and pitfalls, which must be assessed and weighed for optimal use of this technology in the most beneficial and cost-effective way. Furthermore, apart from FDG a variety of radiopharmaceuticals have been introduced to image head and neck cancer, assessing hypoxia (with FMISO, FAZA, Cu-ATSM), tumour cell proliferation (with FLT) or receptor status (with radiolabeled anti-EGFR antibodies). The purpose of these molecular imaging technologies is mainly to characterise tumours and to identify areas of radio- and/or chemoresistance.

*Prostate cancer:* In prostate cancer different PET radiopharmaceuticals are used, as FDG has a limited performance due to the low avidity of prostate tumour cells. The most commonly used radiopharmaceutical in prostate cancer is Choline (labelled with F18 or C11). Choline has extensive evidence in prostate cancer patients with biochemical failure. Choline PET/CT has been applied to radiation treatment planning, both for primary treatment and for the treatment of relapse. Regarding primary treatment, Choline PET/CT is useful (a) at diagnosis for the detection of intraprostatic lesions and (b) for staging helping in patient selection for treatment decisions. With regard to the treatment of relapse, Choline PET/CT can help in the detection of recurrences and treatment monitoring. Furthermore, Choline PET/CT has an important role guiding radiotherapy treatment both of the primary and of the metastases (in cases with oligometastases). Finally, PET/MR can have an added value compared to PET/CT due to the improved sensitivity of MR in detecting bone or bone marrow involvement in prostate cancer. New PET radiopharmaceuticals such as 68Ga-PSMA have shown promising results.

*Liver metastatic cancer:* Advances in 3D-CRT and intensity modulated radiotherapy (IMRT) have enabled high dose radiation to be precisely directed to tumours, subject to a perfect delimitation of the tumour volume to be treated and the anatomical structures which should receive the least possible dose. At the same time, imaging modalities have improved their accuracy in the delimitation of the disease. In liver metastatic cancer, the role of FDG and other radiopharmaceuticals is described.

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## **PET in Lung Cancer**

**Roberto Delgado-Bolton, Logroño**

Lung cancer is the leading cause of cancer related mortality in men and women. The 5-y survival rate for lung cancer varies markedly depending on the stage at the diagnosis. FDG PET/CT is a valuable diagnostic method for non-small lung cancer (NSCLC) for staging, therapy assessment, management and prognosis. Subsequent FDG PET/CT scans performed during follow-up after the completion of the primary treatment can have an added value to clinical assessment and have an impact on management.

In patients with locally advanced lung cancer IIIA (N2), 5-y survival is less than 10% if treated only with surgery. Treatment with induction chemotherapy (Cisplatin) can increase survival. Following induction chemotherapy, FDG PET is an independent prognostic index of pathologic response (R0) and correlates with survival. Most studies perform the FDG PET at the end of the induction therapy but some have performed interim FDG PET, all evidencing the prognostic value of FDG PET. The predictive value of FDG PET has been demonstrated after induction chemotherapy as well as in chemo-radiotherapy. Additionally, following induction chemotherapy, FDG PET helps identifying the patients who would benefit from locoregional control. FDG PET has a correlation with pathologic response as well as with mediastinal restaging, and allows prognostic stratification following induction chemotherapy. However, the European Society of Thoracic Surgeons (ESTS) and the American College of Physicians (ACP) guidelines indicate the need to use invasive techniques to confirm the FDG PET results in these patients.

Recently the prognostic significance of intratumoral metabolic heterogeneity on pretreatment FDG PET/CT patients with lung cancer who were pathologically NO (pN0) after curative surgical resection has been assessed. Metabolic parameters and heterogeneity of the primary tumour on pretreatment FDG PET/CT can predict recurrence in p0 NSCLC of adenocarcinoma type who have undergone curative surgery but not in squamous cell carcinoma type.

Other PET indexes have demonstrated a prognostic value. Total lesion glycolysis (TLG) can predict survival and development of Gefitinib resistance in EGFR-mutant NSCLC patients treated with first-line Gefitinib.

Regarding N-staging, accurate assessment of lymph node (LN) malignancy is critical for staging and management decisions. Adenocarcinoma histology, higher LN SUVmax and higher LN risk category independently

correlate with nodal involvement with malignancy. Furthermore, a study analysing the ratio of lymph node to primary tumour SUV on PET/CT has demonstrated that the ratio is more accurate than SUVmax when assessing nodes of low to intermediate SUV, allowing accurate prediction of nodal malignancy in NSCLC.

FDG PET/CT is also a valuable tool in radiation treatment planning and follow-up. Following stereotactic body radiation therapy (SBRT) in patients with stage I NSCLC, the early detection of recurrences is an important issue, especially in patients with mass-like fibrosis. Characteristics such as the opacity pattern, increasing maximum diameter and SUVmax>5 are indicators of local recurrence. Furthermore, a pre-radiotherapy FDG PET/CT may be used to identify the FDG avid volumes which a higher uptake which correlate with post-therapy persistence of FDG uptake and may benefit of dose escalation.

Another interesting issue is the research focused on 4D imaging. With 4D FDG PET/CT, the addition of co-registered 4D-PET data to 4D-CT based target volume delineation for SBRT of centrally located lung tumours increases the interobserver agreement and may help to avoid geographic misses.

In order to apply FDG PET/CT in monitoring tumour response to therapy, a prerequisite is the repeatability of the quantitative parameters derived from FDG PET/CT studies. A recent study has shown the variability of repeated measurements of tumour FDG uptake is slightly larger than reported in previous studies, although the findings support the definition of tumour response according to PET Response Criteria in Solid Tumors (PERCIST). Another study has shown that metabolically active tumour volume (MATV) measured with 50% of SUVmax corrected for local background is recommended on the basis of a high feasibility and repeatability.

## **Recurrent Thyroid Cancer; what to do?**

***M.P.M. Stokkel, NKI-AVL, Amsterdam***

The incidence of thyroid cancer is rather low compared to lung and breast cancer, but is still increasing. Standard treatment nowadays is surgery and ablation followed by ultrasonography and Tg-off measurements for optimal tumor surveillance. Recurrent disease is commonly observed within 2 to 5 years and, in general, surgery and treatment with radioiodine (I-131) are options for treatment. Additional imaging is required in case of discrepancies between different tests, such as highly elevated Tg-off values and a small lymph node metastases in the neck, elevated Tg levels and negative standard imaging or I-131 post-treatment scans and Tg-antibodies in combination with normal Tg levels. All findings will guide the clinicians to the optimal treatment planning. It is known that FDG PET/CT has established value in many cases and the combination of Tg-values, I-131 scanning and FDG-PET/CT are indicative for dedifferentiation. This phenomenon is observed in 20-50% of the patients with recurrent disease.

Regarding treatment options, the most optimal strategy in recurrent thyroid cancer is I-131 therapy, surgery or a combination of it. I-131 therapy in metastasized disease is indicated as long as uptake or response is observed. Its role after complete lymph node dissection in the neck and normalization of Tg-off levels is less established. In patients with recurrent disease in which I-131 uptake or tumor response to high dose of I-131 is not observed anymore, other treatment options should be applied in which radiotherapy, chemotherapy and targeted therapy are less optimal alternatives.

## **The role of Nuclear Medicine in Breast Cancer imaging: PET/CT or PET/MRI**

***M.P.M. Stokkel, NKI-AVL, Amsterdam***

The incidence and prevalence of breast cancer is worldwide high and still increasing. Due to its histological heterogeneity and different treatment options, optimal characterization and staging is required in which imaging plays an important role. The sentinel node procedure as nuclear medicine technique is an established tool to assess lymph node involvement, and in case of a negative axillary lymph node status, treatment can be initiated. In case of a positive axillary lymph node, additional staging is required in which PET/CT has an increasing role. There are differences in staging performances of PET/CT between lobular and ductal carcinoma, and differences between subtypes of breast cancer (ER, PR and HER2). The most important indication for PET/CT is stage III tumors whereas it is optional, but not recommended yet, in stage II. The value of PET/CT in breast cancer recurrence (restaging) is known being indicative for subsequent treatment. Its role in therapy monitoring is limited, since MRI reveals comparable results. It has to be realized, that it is highly important to use the most optimal imaging technique in which standard PET/CT should be followed by hanging breast PET/CT imaging. It provides more detailed information, better SUV values and images can be compared or fused with MRI. The role of PET/MRI is still limited, but with new tracers and better tools to analyse images, it might become important for other indications than staging, restaging, such as tumor characterization and therapy monitoring. Data in this respect are limited.

## **THE SIGNIFICANCE OF AUTOLOGOUS INDIUM-111 OXINATE LABELLED PLATELETS IN CHRONIC IMMUNE THROMBOCYTOPENIC PURPURA OF ADULTS AND CHILDREN**

**Mila Todorović-Tirnanić**

The method of autologous platelet labelling with In-111 oxinate, and labelled platelets lifespan, production and sequestration site determination at the Center of Nuclear Medicine, Clinical Center of Serbia is the result of 24 years of personal experience in Belgrade and modification and improvement of the original method.

The improved method is described, and the significance of platelet lifespan, sequestration site and production investigation in 555 patients aged from 3,1-83 years, with clinical diagnosis of primary immune thrombocytopenia (ITP), as well as in 6 control healthy subjects is demonstrated.

On the basis of the obtained results, it was possible to confirm diagnosis of ITP in 477 (392 adults and 85 children) out of 555 patients (86 %) with clinical diagnosis of ITP. In 71 patient (69 adults and 2 children) out of 555 (13 %) ineffective platelet production was discovered as the mechanism of thrombocytopenia (patients had normal platelet lifespan, and ITP was excluded), and there were 7 patients (1%) with pseudothrombocytopenia (they had also normal platelet lifespan).

Seventy eight ITP patients were splenectomized after labelled platelets investigation. In all patients (100 %) with spleen or predominantly spleen as platelet sequestration site, splenectomy results were good. In patients with mixed platelet sequestration (in the spleen and liver), splenectomy results were good in 71 %. In ITP patients with hepatic platelet sequestration good splenectomy result was registered in only 20 %, while splenectomy failed in 80 % of patients. On the basis of labelled platelets sequestration site determination, it was possible to predict the efficacy of splenectomy in ITP patients.

This investigation enabled visualization of 18 accessory spleens in 13 ITP patients (in 2,7 % of ITP patients) and their role in thrombocytopenia could be estimated.

Unstable atherosclerotic plaques and acute thrombosis were visualized in ITP patients. Chronic thrombosis could not be registered because of the finished thrombus formation and no more platelet deposition.



## **MIBG in Diagnosis and Therapy of Neuroendocrine Tumors –*looking back and forward***

**Cornelis A. Hoefnagel, Amsterdam**

The clinical use of radioiodinated meta-iodobenzylguanidine (MIBG) for the diagnosis and therapy of tumors derived from the neural crest represents a good example of truly molecular targeting. The development of tracers for the adrenal cortex and medulla and the heart took place at the University of Michigan since the 1960's. After working with  $^{14}\text{C}$ -epinephrine for neuroblastoma and  $^{14}\text{C}$ -dopamine for pheochromocytoma initially, they switched to bretylium analogs and quaternary ammonium derivatives for imaging:  $^{125}\text{I}$ -labelled isomers of iodobenzylguanidine were synthesized by Wieland and he was the first to describe the imaging of the dog's adrenal medulla by  $^{131}\text{I}$ -*para*-iodobenzylguanidine in 1980 and Sisson reported imaging of pheochromocytoma in man by  $^{131}\text{I}$ -*meta*-iodobenzylguanidine in 1981. In Europe  $^{131}\text{I}$ -MIBG with low and high specific activity (for imaging and therapy, respectively) became commercially available and, from 1984 on, several groups reported its successful use for scintigraphy and therapy of pheochromocytoma, paraganglioma, neuroblastoma, carcinoid tumors and medullary thyroid carcinoma. In 1987  $^{123}\text{I}$ -labeled MIBG became available, which had better imaging properties allowing SPECT and proved to be a good agent for studying myocardial sympathetic innervation too. Diagnostic scintigraphic studies using  $^{131}\text{I}/^{123}\text{I}$ -MIBG showed high sensitivity and great specificity in the detection of adrenergic tumors.

Therapeutic results in 534 patients from 14 centers, gathered by the EANM Task Group of Radionuclide Therapy in 1999, demonstrated objective response rates of around 50% in malignant pheochromocytoma, paraganglioma, as well as in children with neuroblastoma, refractory to other forms of treatment. In contrast, in carcinoid tumors and medullary thyroid carcinoma objective responses were fewer, but stabilization of disease, metabolic effects and palliation (in 60% of the patients) were associated with significantly prolonged survival. When, in children with neuroblastoma, the  $^{131}\text{I}$ -MIBG therapy was given at diagnosis, instead of combined chemotherapy, the objective response rate was much higher (around 80%) and the side effects were less.

Despite these good results, a decline in use of  $^{131}\text{I}$ -MIBG for therapy of neuroendocrine tumors occurred with the development of radiolabeled peptide for diagnosis and therapy. Although in the individual patient combined imaging of neuroendocrine tumors using MIBG and octreotide remains the key

to select the therapy with best dosimetric characteristics, in clinical practice, literature and at congresses the use of radiolabeled peptides for therapy is more prominent. Although the indications for both therapies do not overlap completely, also in radiolabeled peptide therapy the objective response rates are relative low (up to 30%) and the metabolic and palliative effects are more pronounced, the latter also having bearing on the survival of patients, as was also observed in  $^{131}\text{I}$ -MIBG therapy of carcinoid tumors.

Then why is therapy using radiolabeled peptides more popular? Certainly the availability of a ideal pair of a PET tracer and a therapeutic agent is an important factor, as high quality PET/CT imaging using  $^{68}\text{Ga}$ -DOTATOC or -octreotate, clearly showing the tumor targeting and biodistribution, is indicative and promotional for treatment with  $^{177}\text{Lu}$ -octreotate.

The similar use of a high quality pair of a diagnostic tracer for PET/CT and/or PET/MR (e.g.  $^{18}\text{F}$ -DOPA and  $^{124}\text{I}$ -MIBG) and a therapeutic radiopharmaceutical ( $^{131}\text{I}$ -MIBG) may bring this way of molecular tumor targeting back into the attention and interest of clinicians. The use of new PET-tracers and hybrid imaging techniques will lead to a reappraisal of MIBG therapy, not in competition with, but parallel to peptide therapy.

## **Nuclear medicine imaging in bone, soft tissue sarcomas (BSTS) and PET/CT impact in their clinical management.**

**E. Piperkova**

***National Oncology University Hospital Center-SHATO, Clinic of Nuclear Medicine, Sofia***

Bone and soft tissue sarcomas (BSTS) are rare mesenchymal tumors, develop from many types of tissue such as bone, cartilage, connective tissue, muscle, fat, peripheral nerves and vessels, comprising approximately 1% of all malignancies with a wide array of histologic subtypes with a large variation in the degree of malignancy and aggressiveness, biologic behavior, which contribute to the difficulty in understanding the natural history and patterns of response to treatment. Most types of high-grade BSTS have a tendency to metastasize haematogenously to the lungs, and metastases to the lymph nodes are uncommon. Often there are no signs or symptoms until the tumor is big and presses on nearby nerves or other parts of the body.

The prognosis of BSTS depends on the true extent of disease and tumor grade in the primary diagnosis. However, after surgical removal, 40% to 60% of the patients develop local or distant recurrence. Accordingly the management and the outcome of BSTS would be improved with the choice of the most accurate diagnostic procedures which allow to image functional and structural behavior permitting an accurate tumor staging, restaging, monitoring of chemo/radiation therapy response, differentiating viable sarcoma from post-treatment changes or benign diseases.

Ultrasound (US), X-ray computed tomography (CT) and magnetic resonance imaging (MRI) define anatomic details at the initial presentation of the disease and are helpful in identifying the extent of the lesions. Unfortunately these methods have some limitations in differentiating tumor recurrence from post-therapy fibrosis or necrosis. Additional problems are caused by the metallic implants commonly used in these patients. Contrast angiography demonstrates malignant angioarchitecture, helpful in differentiating recurrence from fibrosis but it is an invasive technique and also encounters problems in cases where postoperative physiological vascular overgrowth obscures the anatomic structures following surgery or chemotherapy.

**Nuclear Medicine techniques in the diagnosis of brain death**  
**R Mititelu**  
**Dept of Nuclear Medicine**  
**Central University Emergency Military Hospital, Bucharest**

Definition of death from a medical point of view is referred to the stopping of vital organ functions and the irreversible changes which take place, beyond any possibility of resuscitation.

The exact moment of death can be, sometimes, difficult to define in time, and the medical criteria for diagnosis of death have changed over time in a significant way making ethical and legal implication of this diagnosis a major issue. Lately "Brain Death" is a new concept to define death. This is in fact an important issue as there is a need to recover the organs and tissues for transplantation before these suffer irreversible damages to ensure a successful intervention.

Moreover, once diagnosed with a high degree of accuracy and certainty, brain death automatically implies stopping of any resuscitation procedures in intensive care units. Although apparently easy to establish, diagnosis of brain death has major consequences from ethical, philosophic, religious, psychological and forensic point of view and can be, sometimes, difficult to establish. Thus there is a need to establish this in an accurate way by either biochemical tests or appropriate imaging methods.

The present work will focus on the current working protocols in diagnosis of brain death with the help of isotopes and other Nuclear Medicine techniques. It will also review the existing international guidelines the nuclear medicine procedures that can be successfully used in diagnosis of the brain death namely cerebral radionuclide planar angioscintigraphy, potential role of SPECT – CT and PET –CT, and the advantages and disadvantages of using these techniques.

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## **INTRAARTERIAL YTTRIUM-90 MICROSPHERE THERAPY FOR PRIMARY and METASTATIC LIVER TUMORS**

**BOZKURT MF, M.D., F.E.B.N.M.**

Intraarterial Yttrium-90 (Y-90) microsphere therapy for liver tumors is an internal radiation treatment which is performed by providing therapeutic beta radiation from Y-90 loaded microspheres delivered to tumor microcirculation via femoral arterial route. The theoretical basis of this treatment depends on the fact that the blood supply for tumor cells is mostly from hepatic artery while the healthy hepatocytes get their blood supply from portal venous system. Therefore, intraarterial delivery of Y-90 microspheres provides high radiation dose to tumor cells in order to cause radiation damage and because of selective radiation delivery to tumor cells, normal hepatocytes and extrahepatic sites can be protected from some serious side effects of radiation therapy to a great extent. Another major characteristics of this therapy is that the method does not necessarily depend on the tumor type as well as number of lesions and histopathological features of the tumors and it can be applied in the same manner for both primary and metastatic liver tumors. The microspheres used for this therapy can either be resin-based or glass microspheres and they are mostly used in hepatocellular and cholangiocellular cancer as primary as well as colorectal, breast, neuroendocrine and any other tumor which metastasised to the liver as long as it is unresectable. There are increasing number of studies in literature which conclude that intraarterial Y-90 microsphere therapy is a highly effective and safe treatment option which favors both disease-free and overall survival in hepatocellular and colorectal cancer patients with unresectable disease. Y-90 microsphere treatment has been feasible in Turkey since 2008 and so far around 300 patients at Hacettepe University Hospital in Ankara were treated, of whom majority resulted with partial response without any serious side effects and complications.

## **Myocardial perfusion SPECT imaging in abnormal ventricular conduction**

**Rimbu A<sup>1,2</sup>**

- 1. Centre de Médecine Nucléaire, Institute Andrée Dutreix, Centre de Cancérologie et Radiothérapie Nord Littoral, Dunkerque**
- 2. Department of Nuclear Medicine, « Colentina » Clinical University Hospital, Bucharest**

Coronary artery disease (CAD) is the most prevalent form of cardiovascular disease affecting millions of people and being a major public health problem. Over the last decades, single photon emission computed tomography (SPECT) imaging of myocardial perfusion (MPI) has proven an invaluable tool for evaluating patients in cardiovascular medicine and a sensitive tool for detecting CAD. By assessing myocardial perfusion, SPECT imaging aids in diagnosis of CAD and patient risk stratification, providing information on extent of myocardium at risk and scar-myocardial viability, disease progression, hemodynamic significance of coronary artery stenoses and myocardial function using gated-SPECT technique. For the CAD, percutaneous transluminal intervention (PCI) procedures are performed. The relative high occurrence of restenosis, despite stent implementation, seems to be the primary limitation of PCI. SPECT is crucial to differentiate patients with angina from those with exo-cardiac chest pain syndromes, to assess peri-intervention myocardial damage, to predict-detect restenosis after PCI, to detect CAD progression in non-revascularized vessels, to evaluate the effects of intervention if required for occupational reasons and to evaluate patients' long-term prognosis. For a correct interpretation of MPI in all of these situations, it is important to know and detect image artefacts related to both patient and technical factors. False-positive findings on MPI have frequently been identified in the presence of abnormal ventricular conduction, especially in left bundle branch block (LBBB), in right bundle branch block (RBBB), in left anterior hemiblock, after previous coronary bypass surgery etc. The aim of this presentation is to evaluate global and regional gated MPI in the patients with conduction abnormality and or without coronary artery disease.

## **Pain Palliation and Treatment of Refractory Bone Metastases(Prostate and Breast Cancer) with Re-188 HEDP**

**H.J.Biersack,Bonn**

**F.F.Knapp,Oak Ridge**

Therapeutic radionuclides (P-32, Sr-89, Sm-153, Re-186) for bone pain palliation have been used since almost 60 years. In the eighties of the last century, Re-188 HEDP -a cheap generator eluate of Tungsten-188- was introduced into clinical Nuclear Medicine. Carrier-added kit production is easy, and the generator with a shelf-life of approx. 4 months may be shared by several hospitals.

Dose escalation studies have shown that activity amounts up to 90mCi are well tolerated, and if the thrombocytes are over 200.000, up to 120mCi may be injected. The decreases of the blood counts are mild and reversible. If necessary, the injections may be repeated several times.

In 2003, Palmedo et al.(J Clin Oncol) have published data on repeated bone-targeted therapy for hormone-refractory prostate cancer using Re-188HEDP and were able to prove that repeated injections led to improved bone pain palliation(92%) and additionally to an improved survival(12.2 vs.7.0 months). In 39%, prostate specific antigen was decreased by 50%. A follow-up study in 2011(Biersack et al.,J Nucl Med) documented that pain palliation was achieved in over 90% when even more than 2 injections were performed: in patients who had 3 or more injections, the survival could be improved from 9.98+/- 2.21 up to 15.66+/- 3.23 months.

In a group of 60 patients with breast cancer and bone metastases, the same radiotracer had been used and again an improved survival and pain palliation had been observed, however, the groups were too small to draw valid conclusions.

This presentation will be concluded with a short historical highlight: the discovery of Rhenium.

One of the missing elements of the Mendeleev Table, element 75, was discovered by Ida Noddack-Tacke and her husband in 1925, and it was named "Rhenium" in honor of her birthplace near to the Rhine River(lat. Rhenus).



## **ON-LINE TELEMONITORING OF PATIENTS TREATED WITH HIGH DOSES OF RADIONUCLIDE THERAPY. OUR COMPREHENSIVE TELEMEDICINE SYSTEM AS USEFUL TOOL IN CLINICAL PRACTICE**

**Matović M<sup>1</sup>, Jeremić M<sup>1</sup>, Urošević V<sup>2</sup>, Ravlić M<sup>3</sup>, Vlajković M<sup>4</sup>**

**<sup>1</sup>Department of Nuclear Medicine, Clinical Center Kragujevac and Faculty of Medical Sciences, University of Kragujevac**

**<sup>2</sup>Polytechnic School in Cacak, University of Kragujevac**

**<sup>3</sup>Prizma Company, Kragujevac**

**<sup>4</sup>Department of Nuclear Medicine, Clinical Center Nis and Medical Faculty University of Nis**

Following radionuclide therapy, patients usually must remain hospitalised in special restricted access premises until radiation in their body drops below a certain level. During hospitalisation, some of these patients can experiencing some complications or adverse reactions. It is of vital importance that doctor and nurse have audio-visual contact with patients, follow-up their vital functions, and follow-up decline of radiation in their body during hospitalisation. In the other hand, despite strict instructions given to them by physician and nurse before administration of radionuclide therapy, the patients often try to leave "restricted area". In this case we need alarming system in order to achieve prompt alarming of the personnel when such case occurs, and be able to provide adequate measures.

Telemedicine approach could be very useful as solution for all these challenges. We have developed comprehensive telemedicine system which covers four important fields: continuous on-line remote monitoring of patients' vital functions registered with bed side monitor; video surveillance of area which use patients during hospitalisation; continuous on-line monitoring of rest radioactivity in patients body and alarming system dedicated for case when patient attempt to leave the special restricted access premises. Our system consists of own developed hardware/software solutions for data aquisition and processing and established using Internet connection and services.

We used our system for more than 500 patients who received radionuclide therapy. From our experience gained over the past 4 years, this telemonitoring system dedicated for patients receiving radionuclide therapy, ensures a high level of safety for the patient and medical staff.

## **ROLE OF SPECT-CT IN DIAGNOSIS AND DIFFERENTIATION DIAGNOSIS OF BONE METASTASES**

**S.Sergieva**

**Department of Nuclear Medicine, Sofia Cancer Center  
Sofia**

Metastatic involvement is a common occurrence in patients with oncological diseases. Skeletal metastases are clinically important because of the associated symptoms and complications leading to the tumor-induced bone disease and their profound significance for staging, treatment and prognosis. The frequency with which metastases are detected varies considerably with the type of primary tumor and with the methodology utilized for detection. Whole body bone scintigraphy (WBBS) is the most sensitive method for early detection of secondary skeletal lesions; it is positive with infiltration of 5-15 % of the trabeculae. The specificity of this technique, however, is low due to the fact that increased mineral metabolism is observed in a number of benign diseases of degenerative, inflammatory or traumatic character. The combined application of baseline WBBS, followed by more specific techniques such as SPECT-CT fusion is an advanced approach for diagnosis and staging of osseous metastases.

The most important clinical application of bone SPECT-CT imaging is for differential diagnosis between degenerative and metastatic foci with abnormal tracer uptake and similar scintigraphic appearance on the WBBS. SPECT-CT allows a significant increase in diagnostic accuracy, mainly because of the improvement in specificity determined by CT, having capability to describe as definitely benign or definitely malignant more than 90% of the findings, which had been classified as indeterminate on planar scans. CT is a valuable method for characterizing destruction of the bone spongy lesions, their consolidation or calcium accumulation. This fact allows differentiation of the osteolytic metastases from the sclerotic and mixed ones. This is possible because of the good differentiating ability of CT. It has direct relation to the therapeutic approach of tumor-induced bone disease by determining the necessity for or prescribing diphosphonate medication, metabolic radiotherapy or external beam radiotherapy. Hybrid SPECT-CT technique may also improve WBBS sensitivity because of the possibility to detect "cold" osteolytic lesions with soft-tissue component, usually not showing tracer uptake on the bone scintigraphy. These type of bone lesions were observed predominantly in patients with renal, lung, colorectal, endometrial or urinary bladder cancer.

They were not visualized clearly on the WBBC because of the absence of osteoblastic reaction and respectively low tracer uptake. SPECT-CT was applicable for exact localization of abnormal lesions in the bones, their morphological type, size and extension, especially in cases with superposed activity from the urinary bladder over the pelvic structures. WBBS followed by SPECT-CT is a very effective diagnostic approach to follow up patients with osseous metastatic lesions after complex therapy in order to obtain therapeutic response.

**Read the small letters of the Guidelines for ablation therapy and apply them to the patients. Size does not always matters.**

**SavvasFrangos MD, FEBNM, Nuclear Medicine Specialist**

There are many guidelines and recommendations suggesting ablation therapy in differentiated Thyroid Carcinoma (DTC). Most of them are concentrating on the size of the tumor.

This presentation will be focused on the details of the guidelines and recommendations.

We will find that at least one set of recommendations suggests the need of ablation to a large part of the patients with DTC smaller than 1 cm.

We will examine the following guidelines and recommendations: EANM, NCCN and ATA.

Moreover, the ETA and SNMMI recommendations will also be taken into consideration.

The presentation will be supported by data of a retrospective, two-centre quality assurance study on patient and treatment characteristics from a large cohort of patients treated on two tertiary referral centers within the European Union, more specifically Cyprus and Greece.

Using separately each of the guidelines different numbers of patients without indication for ablation came out each time: using ATA guidelines 38.7% of the patients have no indication, using NCCN guidelines 25,6% showed no indication and using EANM guidelines 19,3%. The study was using combination of all guidelines and only 18,5% have had no indication for ablation. Using the study's criteria only 10 patients out of 326 had no indication for ablation and 6 of them had positive anti-thyroglobulin antibodies.

Putatively “low-risk” DTC patients frequently had high-risk or unclear risk characteristics, suggesting that “selective” radioiodine ablation in such patients may seldom be applicable outside international centres of excellence. Proxies for surgeon experience and surgical completeness correlated with remnant number/uptake intensity, suggesting that these variables may aid ablation-related decision-making.

## **IMAGING IN CHILDREN WITH URINARY TRACT INFECTION URINARY TRACT INFECTION**

**Ajdinovic B**

**Military Academy, Belgrade**

Urinary tract infection (UTI) is a common pediatric problem with the potential to produce long-term morbidity. Young children presenting with fever may have nonspecific symptoms of UTI, and a high index of suspicion is appropriate in this setting, as bacteriuria would indicate a high probability of upper tract infection. The need for imaging in children with febrile UTIs is debated in search for a balance between reducing hospitalization, cost and irradiation but nevertheless minimizing renal damage.

The standard imaging studies for children presenting with UTIs initially included noninvasive ultrasound and voiding cystourethrography (VCUG) („bottom up approach“). However, the ultrasound is neither sensitive nor specific for diagnosing vesicoureteral reflux. Although some studies suggest that it is of limited value, most physicians believe that it is an appropriate screening test to rule out major abnormalities. High-quality ultrasounds, often performed in the last trimester of pregnancy, identify significant congenital abnormalities, and the yield of a further ultrasound may be low if prenatal results were normal. The VCUG has been used consistently since the 1960s and can be performed as a standard contrast study or with a radionuclide. Typically, the contrast study is chosen for the first study due to its greater anatomic detail, although the radionuclide cystogram has been shown in some studies to have a higher sensitivity. While no test is perfect, there is little question about the VCUG's ability to detect reflux. However, questions have been raised about whether routine work-up with VCUG is the best strategy to improve long-term outcomes, given a lack of evidence to support the benefit of prophylactic antibiotics once reflux is diagnosed. In addition, newer research has demonstrated the presence of renal scarring in the absence of reflux, which has led to interest in other imaging modalities. Renal scans have been used to evaluate children with UTIs since the 1980s, and their sensitivity and specificity for pyelonephritis have been well documented. A substantial number of defects on DMSA scans occur in the absence of reflux. This has led some to recommend that if renal scarring is to be avoided, a renal scan should be the initial investigation in a child with a UTI to detect those at greatest risk for a persistent scar („top down approach“). Unfortunately, many studies do not have complete enough follow-up to determine the true incidence of scarring, as it has been shown that defects will

change up to 6 months later. As discussed earlier, the ramifications of renal scarring for the risk of long-term morbidity such as hypertension and renal failure are also unclear. Further research with long-term follow-up will be necessary before physicians feel comfortable using a DMSA scan as the primary study to determine further management in a child with a first UTI. Different guidelines have been recently published.

The appropriate work-up after a UTI in a young child or infant currently includes a renal ultrasound with/without a VCUG. Further research may define whether routine performance of these tests improves outcomes or whether more selective use or other tests such as DMSA may be a more effective approach.

## **Clinical Impact of ventilation/perfusion single-photon emission computed tomography in detection of pulmonary embolism and follow up**

**Amela Begic**

**Clinic for Nuclear Medicine Clinical Centre, University Hospital Sarajevo, Sarajevo**

Pulmonary embolism (PE) can only be diagnosed with imaging techniques, which in practice is performed using ventilation/perfusion scintigraphy (V/P scintigraphy), or multi-detector computed tomography of the pulmonary arteries (MDCT). V/P scintigraphy for diagnosis of PE is universally available but imaging protocols and interpretative strategies show large variation. Unfortunately, the large Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED I) showed a high number of non-diagnostic examinations (65%) due to the not standardized method, the stiff and probabilistic interpretation criteria that were confusing to the clinicians. Bajc et al. validated ventilation/perfusion single photon emission tomography (V/P SPECT) for diagnosis of PE on pigs, and showed the superior value of V/P SPECT over V/P planar imaging. Clinical studies showed similar results as validated on pigs by many authors (Bajc et al, Reinartz et al. Gutte et al. Quirice et al.). Latest study by Gruninget. al. also confirmed high sensitivity of V/P SPECT of 95.7%, specificity 98.6%, positive predictive value 95.7%, negative predictive value 98.6% on about 2000 examinations. V/P SPECT images have documented value also over CT. The PIOPED II study showed sensitivity of MDCT for PE of only 78% and high proportion of false positive study (45%) in patients with low clinical probability. The strength of V/P SPECT is in the new interpretation criteria with clear answer to the clinicians regarding PE. To be clinically useful, interpretation of an imaging test should be affirmative or negative with respect to PE (PE: yes or no) and should not be based on probability categories. European Nuclear Medicine Guidelines recommend V/P SPECT as a first choice method for diagnosis of PE and follow-up, due to the high negative predictive value, high sensitivity and specificity, feasibility in almost all patients and low radiation exposure. V/P SPECT allows also quantification of the PE extent which might be used to personalize treatment such as outpatient and inpatient treatment. Furthermore, Begic et al. showed that significant resolution of mismatched perfusion defects occurred between V/P SPECT controls within the first 3 months of anticoagulation ( $p < 0.001$ ) but not thereafter. It is therefore recommended that V/P SPECT follow-up should be considered at 3 months after diagnosis. The authors recently reported that tailoring anticoagulant treatment

is feasible by incorporating V/P SPECT in the clinical decision tree.

## **PREDICTION OF SENTINEL LYMPH NODE STATUS BY PATIENT'S AND PRIMARY TUMOR CHARACTERISTICS IN CUTANEOUS MELANOMA - A SINGLE CENTER STUDY**

**Jaukovic L<sup>1</sup>, Rajovic M<sup>2</sup>, KandolfSekulovic L<sup>3</sup>, Radulovic M<sup>1</sup>,  
Zlotarevski L<sup>4</sup>, Ajdinovic B<sup>1</sup>, Novakovic M<sup>2</sup>**

**<sup>1</sup>Institute of Nuclear Medicine, <sup>2</sup>Clinic for Plastic and Reconstructive Surgery,  
Clinic for Dermatology, <sup>4</sup>Center of Pathology and Forensic Medicine  
Military Medical Academy, Belgrade**

**OBJECTIVE** Aim of our study was to identify patient's and primary melanoma characteristics predictive of positive SLN biopsy result in our population.

**METHODS** Retrospective review of 126 patients with malignant melanoma who underwent SLN biopsy, was performed. To delineate the relation of each variable with positive SLN status, we examined all variables by univariate logistic regression with odds ratios representing effect size. We performed multivariate regression analysis using only the factors that were significant in the univariate analysis.

**RESULTS** In all, 21.4 % of patients had one or more positive SLNs. Breslow thickness, primary melanoma localization, and the presence of lymphovascular invasion were the all significant predictors of SLN status on univariate analysis. Body site location was a significant predictor of SLN positivity in univariate as well as in multivariate model. Trunk localization was the significant factors in predicting negative SLN when comparing trunk location to all the other locations. Acral location of primary melanoma almost tripled the odds of SLN positivity (OR = 2.80) compared with location on the head/neck. Multivariable analysis with 126 cases included in model revealed Breslow thickness and primary tumor localization to be significant independent predictors of SLN status ( $p < 0.05$ ). The third variable regressed (LVI), was no more significantly associated with SLN status.

**CONCLUSION** Beside the well established primary tumor thickness as the predictor of SLN positivity, we observed significant association between body site location and lymphovascular infiltration. Our findings on possible relation between the acral localization and SLN metastasis require further clarification.



## **ARTEFACTS AND PITFALLS IN MYOCARDIAL PERFUSION IMAGING**

**Qaisar H. Siraj**

Myocardial perfusion imaging is a powerful tool in the diagnosis and prognosis of coronary artery disease. Nuclear cardiac imaging involves a succession of stages, procedures and operations. This cascade of multidisciplinary processes is essential to the production of high-quality images. In order to consistently obtain optimum quality images, one should not only be cognizant of the idiosyncrasies of the equipment and software, but should constantly on the alert against various underlying causes of erroneous or inconsistent scan results, which may affect the quality and interpretation of individual images.

The inherent complexity of myocardial imaging and the multiple steps involved in the process makes it vulnerable to a number of pitfalls that might originate from radiopharmaceutical preparation and patient administration to image acquisition, processing and display. Not surprisingly, a significant proportion (15-25%) of cardiac scans are associated with attendant artifacts. A knowledge and awareness of the multiple sources of artifacts, either patient-related or technical in nature, is therefore essential to enable the identification, timely correction and prevention of such artifacts.

Prospectively, the technique and methodology should be optimized and tailored to the individual being investigated; retrospectively, knowledge of various sources of errors that impact on image quality is important for correct interpretation. Identification and correction of artifacts is essential to obtain high standard diagnostic studies.

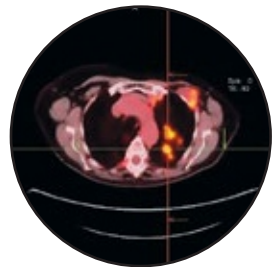
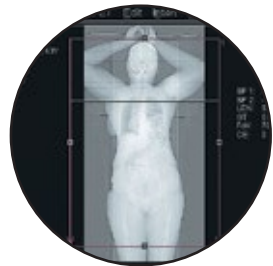
## **Quality Assurance and Quality Control of Nuclear Medicine Equipment – SPECT/CT Systems**

**Dimcheva M, Sergieva S, Jovanovska A**

**Department of Nuclear Medicine, Sofia Cancer Center, Sofia**

**INTRODUCTION:** Quality Assurance of SPECT/CT gamma cameras requires a careful handling of the measured Quality Control data. Quality control procedures are required to ensure that nuclear medicine equipment is functioning correctly. The regular quality control tests are intended to detect problems of the systems before they impact on clinical patient studies. The aim of this work was to present a comprehensive set of test procedures including acceptance testing and regular quality control procedure. **METHODS:** The quality control procedures for SPECT/CT should incorporate both CT and SPECT components and each parameters working limits should be considered. In addition, for SPECT/CT, a check on the alignment between the CT and SPECT modalities should be performed periodically. Such a gantry alignment check should determine any offset between the CT and SPECT modalities to be incorporated into the fused image display to ensure accurate image alignment. The selection of the tests is discussed and the tests are described; some results are presented. **RESULTS:** The results of the acceptance tests should be recorded as a base against which to compare future tests. Routine quality control measurements should be made at regular intervals, and also after any major change of components, updating by the manufacturer, or repairs. **CONCLUSIONS:** With this set of test procedures each nuclear medicine department should be able to perform regular quality control of their SPECT/CT systems. All clinically used equipments should be objects for quality control to ensure the correctness of the measured values.

# FIRST PET-CT CENTER IN THE REGION



## CIRCULATING TUMOR CELLS A NEW PROGNOSTIC FACTOR IN MINIMALLY INVASIVE FOLLICULAR THYROID CARCINOMA

Doina Piciu

Institute of Oncology “Prof.Dr.Ion Chiricuță”, Department of Nuclear Medicine and Endocrine Tumors, Cluj-Napoca

**Introduction:** Follicular thyroid carcinoma (FTC) is a well-differentiated carcinoma, with an incidence of 5-15 % worldwide. FTC has been classified as minimally invasive (MIFC) or widely invasive carcinoma (WIFC), according to histological criteria.

**Objectives:** The aim of this study was to determine the presence of circulating tumor cells (CTC) in the blood of patients with MIFC, in order to define the treatment and the prognosis.

**Methods:** Between January-June 2015 we conducted a study on 16 cases MIFC, who underwent total thyroidectomy. At one month after the surgery we recorded: gender, age, histological features, tumor size, serum thyroglobulin (Tg) and CTC from venous blood on an immunomagnetic segregation method.

**Results:** Females were 81.3%; the mean  $\pm$  SD age was 47.2  $\pm$  15.79 years. The tumor size mean  $\pm$  SD size was 2.2  $\pm$  1.74 cm; 5 patients had tumor size  $<1$  cm; 5 patients presented capsular and vascular invasion, 4 only capsular invasion; 10 patients out of 16 had CTCs present one month after surgery, with values ranging between 1 CTC/6ml to 13 CTC/6ml. This study shows the CTC value related with the type of invasion. Patients with a change in CTC status from positive to negative had a good prognosis as well as patients without baseline CTC.

**Conclusion:** This study opens the opportunity to improve the management of MIFC making the status of CTC part of the therapy algorithm. Further studies are needed to determine the accuracy of the test and its role in the long-term follow-up.

## **Parathyroid Imaging and Invasive Techniques**

**Seyfettin Ilgan, MD**

### **Parathyroid Imaging**

PHPT is the most common cause of benign hypercalcemia resulting mainly (80%–85% or more) from sporadic, single parathyroid adenomas, followed by hyperplasia, double adenomas and parathyroid carcinoma. Surgery continues to remain the mainstay of treatment for PHPT. While there is still an important role for formal bilateral neck exploration, unilateral focused surgical approach (minimally invasive parathyroidectomy, MIP) has gained wide acceptance in cases of solitary parathyroid adenomas, which is the most common scenario. Several authors have shown that MIP leads to decreased operative time, lower hospital costs, shorter length of stays and fewer events of transient hypocalcemia with cure rates equal to bilateral neck exploration (95%).

Obviously the success of MIP is strongly dependent on accurate preoperative imaging techniques that can predict the presence of single gland disease. Imaging with high-resolution US and dual phase scintigraphy with Tc-99m MIBI are currently favored localization studies with high sensitivities (85%) in identifying hyperfunctioning parathyroid glands. Especially concordant results of both studies correctly identify the single adenoma in 95% of cases. It has been reported that the combination of US and planar scintigraphy had 96% sensitivity, 83% specificity, 88% positive predictive value and 94% negative predictive value for parathyroid localization.

Measuring PTH in the needle aspirate of the suspicious lesions when scintigraphy and US are inconclusive or discordant could make confirmation of the parathyroid origin of a suspicious lesion. It has been reported that PTH assay in needle aspirates is a simple and highly specific method and show superior performance in comparison with parathyroid scintigraphy or US alone.

Retention of Tc-99m MIBI during scintigraphy has been shown to be the most dependable finding to localize parathyroid adenomas. However, MIBI retention is not parathyroid specific and epithelial cells rich in mitochondria could show increased uptake causing false-positive results such as oncocytic tumors and autonomous thyroid adenoma. Blood vessels, esophagus, longus colli muscle, brown fat, enlarged lymph nodes, lymphoma and other malignancies reported among other rare sources of false positive results. On the other hand, small parathyroid adenomas, oxyphil cell content, and necrosis are known reasons causing false-negative scintigraphic results.

Other imaging or localization studies including computed tomography, magnetic resonance imaging, positron emission tomography and selective venous sampling are mainly recommended in patients with negative scintigraphy and US studies and persistent or recurrent PHPT.

Despite comparable sensitivity with scintigraphy the principal limitation of US is its inability to localize the ectopic parathyroid adenomas that lie outside the neck in small percentage of patients (<2%) with PHPT.

The sonographic features of parathyroid adenomas have been described in the imaging literature. Parathyroid adenomas are typically markedly hypoechoic, extrathyroidal masses with well-defined margins located posterior to the midportion of the thyroid gland (superior parathyroid) or inferior to the lower pole of the thyroid (inferior parathyroid). Small adenomas are usually ovoid and often lie parallel to the long axis of the neck. Large adenomas may have a lobulated appearance. On color Doppler sonography, the presence of a peripheral vascular arc arising from the inferior thyroid artery branches and enlarged feeding arteries are characteristic. Differential diagnosis of typical and atypical parathyroid lesions will be discussed with video presentations during the lecture.

## **Invasive Techniques**

### **FNAB**

Complete evaluation of the thyroid nodule requires the use of both ultrasound and US guided FNA. Use of ultrasound has been found to alter the clinical management in almost two thirds of cases. Even so, FNA is still considered the single most useful evaluation method for a thyroid nodule. The widespread use of FNA has resulted in great reduction in the number of benign thyroid surgeries while increasing the percentage of cancers found within the surgical specimens.

Beside cytological examination of FNA material, measurement of Tg, PTH and calcitonin in FNA washout provide great contribution of differential diagnosis of lymph node metastasis of thyroid cancer, parathyroid adenoma and medullary carcinoma, respectively.

### **ROLL Technique**

ROLL is a new localization technique which is originally described for non-palpable breast lesions. Technique depends on direct inoculation of small quantity of Tc-99m labeled particles (macroaggregated albumin, colloid etc.) into the lesion under radiographic or ultrasonographic guidance. Recently, ROLL technique, was used for non-palpable nodal recurrences of thyroid cancer in

lateral and central cervical compartments as well as single parathyroid adenoma. Since ROLL technique does not depend on the systemic application of the radiotracer and existence of concentrating ability of lesions, we found this technique extremely helpful in selected clinical problems in cervical region. Furthermore it provides best possible lesion to background count ratio during radioguided surgery with negligible radiation doses to the both operator and patient. We therefore use ROLL technique on a routine basis in patients with PHPT as well as recurrent papillary thyroid carcinoma in central and lateral cervical compartments.

## **Gamma Probe Guided Parathyroidectomy**

**Prof. Dr. Ömer Uğur**

**Hacettepe University**

**Ankara**

**ougur@hacettepe.edu.tr**

With the introduction of sestamibi localization, and the identification of parathyroid adenoma location, the era of focused exploration or minimally invasive parathyroidectomy began. The different techniques associated with focused/minimally invasive parathyroidectomy include gamma probe-guided exploration, and novel endoscopic techniques. The sophisticated techniques of parathyroid imaging allow the surgeon to plan a localized exploration designed to remove the common single focus of disease. The incision is small, dissection is minimal, postoperative pain is less, and hospital stay is shorter. The use of an intraoperative gamma probe facilitates the surgical exploration. The operation could be performed through a smaller incision. The surgeon can locate the abnormal gland readily in the direction of the probe tip where a hot spot is identified. The identification of the parathyroid adenoma is more challenging than it is for sentinel node localization. Background activity in the thyroid gland is significant and the target to background activity ratio is variable depending on both the thyroid and parathyroid washout rates of sestamibi. The gamma probe is only helpful when there is a statistically significant differential between the thyroid and parathyroid count rates. The use of sophisticated protocols calculating the maximum parathyroid to thyroid uptake ratio, thus the optimal time to surgery, increases the success of gamma probe-guided parathyroidectomy.



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## **EVALUATION OF BONE TUMOURS WITH $^{99m}\text{Tc}$ -MDP/MIBI SCINTIGRAPHY**

**Miladinova D. MD PhD, Stefanova M. MD MSc**

**Institute of Pathophysiology and Nuclear Medicine Acad.Isak S.Tadzer, Faculty of medicine, University SsCyril and Methodius, Skopje**

Bone imaging is one of the most versatile and time proven nuclear medicine procedures. Although non-specific  $^{99m}\text{Tc}$ -MDP bone scan (BS) remains one of the primary means of investigation in the evaluation of bone tumours(BT). Any patient with a lesion suspicious of BT should undergo BS, that could be helpful in diagnosis of undetermined cases and as a basic scan before the initiation of different treatment modalities. Tumor-seeking radiopharmaceuticals ( $^{201}\text{Tl}$  chloride,  $^{99m}\text{Tc}$ -MIBI) are commonly used as an additional tool in the investigation of BT.

Our study group was comprised of 30patients (18 with benign-BT and 12 with malignant tumours MT). Each patient underwent three phase bone scanning with MDP. After 3-7 days was performed  $^{99m}\text{Tc}$ -MIBI scan(MS) (with early phase 10minutes and late phase 60minutes after the application). BS and MS were evaluated by visual and semiquantitative analysis. The ratio of the counts of the lesion to the contralateral normal area (T/N) was calculated from the region of interest drawn on BS and MS.

Visual analysis revealed statistically significant difference in MS between BT and MT ( $p<0.05$ ) compared with BS ( $p=0.3408$ ). T/N ratio was significantly higher in MT ( $4.91\pm 2.84$ ) than in BT( $3.67\pm 3.34$ ) on BS, as well on MS where T/N was higher in MT ( $2.71\pm 1.41$  on early and  $2.25\pm 1.02$  on late phase) than in BT ( $1.34\pm 0.46$  and  $1.22\pm 0.28$  respectively).

The sensitivity, specificity, accuracy, positive predictive value and negative predictive value of MS in MT were 91.7, 72.2, 80, 68.6 and 92.9%, compared with BS (100, 33, 60, 50 and 100% respectively).

MIBI scan(MS) could be used as an additional diagnostic imaging method in distinguishing between MT and BT of the skeletal system, by applying visual and semiquantitative analysis of BS and MS. Although it cannot replace tissue biopsy as a definitive diagnostic modality its role is justified in the preoperative evaluation of patients with BT, as well as in the evaluation of the therapeutic response on different treatment modalities.

## **Prognostic importance of SPECT MPI**

**Venjamin Majstorov**

**Institute of Pathophysiology and Nuclear Medicine, Medical Faculty,  
University Ss' Cyril and Methodius, Skopje**

SPECT Myocardial Perfusion Imaging (MPI) is well established nuclear technique for prognostic assesment of patients with diagnosed Coronary Artery Disease (CAD) or suspicion of CAD. Most important predictors of cardiac events that can be measured with SPECT MPI are extent of ischemia, transient ischemic LV cavity dilation and regional and global parameters of LV function on post-stress gated-SPECT images. It has been shown that after adjustment for clinical characteristics, exercise ECG data and rest LV ejection fraction, ischemic burden was independent predictor for all cardiac events.

Patients with normal SPECT MPI have excellent long-term survival rate. Nevertheless, in special populations such as diabetic patients, patients with chronic renal disease and elderly, normal scan has more limited prognostic information in the long run. Increased risk after a normal scan was also observed in patients undergoing pharmacologic stress and with previous CAD.

Generally speaking, the more extensive and severe the perfusion abnormalities on MPI, the worse prognosis and outcome of the patients are. It has also been demonstrated that additional data derived from gated-SPECT, such as poststress LVEF and LV end-systolic volume, provided incremental prognostic information in prediction of cardiac death over perfusion abnormalities alone.

The primary advantage of SPECT MPI over other imaging modalities is its ability to insure functional assessment of CAD. Identifying patients with hemodynamic significant CAD enables selection of patients who will benefit most from myocardial revascularization, not solely identifying those with increased risk.

## **Thyroid ultrasound-basic considerations, US features of benign thyroid diseases and US evaluation of thyroid nodules and neck lymph nodes**

### **Venjamin Majstorov**

Institute of Pathophysiology and Nuclear Medicine, Medical Faculty, University Ss' Cyril and Methodius, Skopje

Thyroid ultrasound (US) is by far most employed imaging modality in patients with thyroid diseases. It is quite simple technique, easy to use, widely available and both comfortable and safe for the patient. US characteristics of normal thyroid gland were discussed. In diffuse thyroid diseases ultrasound is helpful in establishing correct diagnosis and overview of US findings in several benign thyroid diseases was given.

For purposes of risk stratification of thyroid nodules thorough understanding of US features associated with malignancy is needed. Most important US features of malignant thyroid nodules are: hypoechogenicity, irregular or blurred margins, presence of microcalcifications, central vascularisation and AP diameter > TR diameter ("taller than wide") in axial plane. However, some 20-30% of all thyroid carcinoma are isoechoic or hyperechoic, predominantly follicular or Hürthle cell carcinoma. Albeit no single US feature is predictive of thyroid cancer, they help in selection of the nodules for fine needle aspiration biopsy and clinical decision making. Combination of several suspicious features rise the probability for malignancy.

Metastasis in cervical lymph nodes are common in differentiated thyroid carcinoma (DTC). Most affected is central compartment, thereafter lateral neck compartment. US differentiation of malignant from benign neck lymph nodes is important in preoperative assessment as well as in the follow up of the patients with DTC. Several US features may be indicative of malignant lymph nodes, such as round shape of the node, loss of hilum, central vascularisation, microcalcifications and cystic change.

Despite the fact that is relatively simple, thyroid US requires specific training and experience in order to be aware of the spectrum of different ultrasonographic appearances of common focal and diffuse thyroid diseases.

## **LUTETIUM-177 LABELED RITUXIMAB : OPENED GATEWAY TO BETTER RADIOIMMUNOTHERAPY**

**Smilkov Katarina<sup>1</sup>, Gorgieva Ackova Darinka<sup>1</sup>, Janevik ivanovska Emilija<sup>1</sup>, Chinol Marco<sup>2</sup>, Carolo Angela<sup>2</sup>, Gjorgoski Icko<sup>3</sup>**

**<sup>1</sup>Faculty of Medical Sciences, “GoceDelcev” University, Stip**

**<sup>2</sup>European Institute of Oncology, Milan**

**<sup>3</sup>Faculty of Natural Sciences and Mathematics, University “Ss. Cyril and Methodius” Skopje**

The beginning of the new century brought approval of two monoclonal antibodies for therapy of Non Hodgkin'sLymphoma (NHL), Bexxar® and Zevalin®, and opened the gateway to the research in targeted therapy of, mostly haematological malignanices. Since then, the research has been directed toward improvement in three principal, but interdependent factors: the antibody, the radionuclide, and the target tumor/host. Among the most researched anti-CD 20 monoclonal antibodies is rituximab, and among the radionuclides, <sup>90</sup>Y, <sup>111</sup>In, <sup>64</sup>Cu, <sup>153</sup>Sm, and <sup>177</sup>Lu –labeled antibodies have been described or are under development.

The aim of our research was to develop a new lyophilized kit, ready-to label with Lu-177, with a potential to be used in diagnostic and therapeutic purposes. In our experiments, we used rituximab, purified from a commercial preparation, Mabthera®, that was conjugated using *p*-SCN-Bn-DOTA, *p*-SCN-Bn-DTPA and 1B4M-DTPA as chelating agents. The lyophilized kit was prepared in three-day lyophilization protocol. The radiolabeling of the lyophilized kits was performed after reconstitution in 0.9% NaCl, in the presence of acetate ions at pH 7.0 with Lutetium-177 with specific activity of 555 GBq/mg, at room temperature. The radiochemical purity was determined using size-exclusion (SE-HPLC). The results showed preserved antibody structure and suitability for successful radiolabeling with over 95% radiochemical purity in all three radioimmunoconjugates, encouraging further evaluation experiments. Regarding the results obtained, further experiments will be performed in order to demonstrate their biological and pharmacological properties.

## PET RADIOPHARMACEUTICALS IN ONCOLOGY – NEW CHALLENGES IN THE NEW FACILITY

Emilija Janevik-Ivanovska

Faculty of Medical Sciences, Goce Delcev University Stip

Positron emission tomography is one of the most recent and most promising methods of detecting oncological, cardiological and neurological diseases. The technique has the key advantage of enabling diagnosis of diseases in the early stages, determining the extent of the disease process and its pathological impact, as well as monitoring the effectiveness of chemotherapy. In the same time positron-emission tomography (PET) is a powerful tool for imaging and quantifying cellular and molecular processes in humans and has enormous potential to increase our understanding of the pathophysiology of human tumors and to support the development of anticancer drugs.

The University Institute for Positron Emission Tomography is under official establishment as a unique facilities in the country and in the Balkan Region. The new facility is result of the Government investment and joint project with IAEA.

The new facility has Department for Production including cyclotron for production of ultra-short-lived isotopes (F-18, C-11, N-13 and option for solid targets), two full GMP production laboratories for PET radiopharmaceuticals, one completely dedicated for FDG production and second include production of other F18, C-11, N-13, Ga-68 radiopharmaceuticals and Cu-64 (solid targets) in a future. The third production laboratory that is part of the same GMP production site is dedicated for small scale production of therapeutical radiopharmaceuticals for clinical trials and investigation. The integrated part are two QC laboratories and one research laboratory for preclinical investigation including toxicological studies of new radiopharmaceuticals, especially dedicated to oncology.

According to the National Guidelines (Figure 1) that incorporate from European, IAEA and internationally accepted guidelines, and also reflect consensus opinion concerning the diagnostic procedures to be employed in the majority of cancers for most patients, PET center will start to produce following radiopharmaceuticals:

- $^{18}\text{F}$ -Fluorodeoxyglucose ( $^{18}\text{F}$ -FDG)- for different tumors and for imaging inflammation, infection and brain function
- $^{68}\text{Ga}$ -DOTA analogues - mainly used to image neuroendocrine tumors, pheochromocytoma, paraganglioma or neuroblastoma.
- $^{18}\text{F}$ -sodium fluoride – for standard bone scintigraphy
- $^{11}\text{C}$ -Choline mainly used for imaging prostate cancer

- $^{13}\text{N}$ - Ammonia – for imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease.

The new Institute for Positron Emission tomography will be a multi university institution of global standing, with distinctive strengths in education and research using extensive suite of state-of-the-art produced radiopharmaceuticals as imaging tools.

## **RADIONUCLIDE ANTIBODY-CONJUGATES: DEVELOPMENTS AND APPLICATIONS TO OBTAIN A TARGETED CANCER THERAPY**

**Gjorgieva Ackova Darinka<sup>1</sup>, Smilkov Katarina<sup>1</sup>, Petre Makreski<sup>2</sup>, Trajče Stafilov<sup>2</sup>, Duatti Adriano<sup>3</sup>, Janevik-Ivanovska Emilija<sup>1</sup>**

<sup>1</sup>Department of Pharmacy, Faculty of Medical Sciences, University Goce Delčev – Štip

<sup>2</sup>Department of Chemistry, Faculty of Natural Sciences and Mathematics, University “Ss. Cyril and Methodius” – Skopje

<sup>3</sup>Department of Chemical and Pharmaceutical Sciences, University of Ferrara, Ferrara

Understanding the behaviour and function of biomolecules at the molecular level is key to the discovery and development of new drugs, as well as diagnostic techniques. The characterization of therapeutic monoclonal antibodies (mAbs) poses many challenges compared to those of low-molecular mass drugs because of their inherent complexity due to their protein nature. Achievements in this field of science have changed the way that drugs are being designed and developed nowadays. Vibrational spectroscopy techniques, like Fourier Transform Infrared (FTIR) spectroscopy and Raman spectroscopy (RS) have helped to determine the secondary structure of complex protein molecules, as well as protein-ligand complexes. Other advantages of these techniques include the need of very low sample concentration and the ease of sample preparation. Therefore, they are gaining growing importance in the field of medicine and pharmacology.

Our group has demonstrated the use of these tools to understand protein-ligand interactions in therapeutically important mAb, rituximab, conjugated with three different bifunctional chelating agents (*p*-SCN-Bn-DOTA, *p*-SCN-Bn-DTPA and 1B4M-DTPA) with no available structural information of obtained complexes. A special interest was directed to the secondary structure of the antibody. In spite of the fact that Raman spectra show characteristic fingerprints which can be used for molecular identification, we detected the most important protein groups, and noted the  $\alpha$ -helix and the  $\beta$ -sheet structures in the molecule.

The high-throughput approach presented here has significant potential for analyzing the stability of biotherapeutics as well as any other biological molecules which are used as anti-cancer therapeutic drugs.



## **Imaging of the cardiac autonomous nervous system**

**Riemer H..A. Slart, MD, PhD**

**Nuclear Medicine Physician, staff member of the department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen**

$^{123}\text{I}$ -MIBG SPECT is many used for imaging the cardiac nervous system in the past. The high spatial and temporal resolution of PET enables noninvasive quantification of neurophysiologic processes at the tissue level. PET ligands for catecholamine receptors, along with radiolabeled catecholamines and catecholamine analogs, have been applied to determine involvement of sympathetic dysinnervation at different stages of heart diseases such as ischemia, heart failure, and arrhythmia.

This lecture summarizes the background of  $^{123}\text{I}$ -MIBG application in cardiology and the pallet of different and novel pre-synaptic and post-synaptic PET tracers and its potential value in clinical neurocardiological imaging.

## Management of juvenile differentiated thyroid carcinoma: 37-years experience in Serbia

Jasna Mihailovic

Department of nuclear medicine, Oncology Institute of Vojvodina, Sremska Kamenica

Juvenile differentiated thyroid carcinoma (DTC) is a rare neoplasm, accounting for 0.5%–3% of all childhood malignancies. It appears in 2–10% in patients aged  $\leq 20$  years. Incidence in pre-pubertal period is 1% and 7% in adolescent period. According to the Serbian Cancer Registry 42 newly diagnosed DTC patients aged  $\geq 19$  years were reported during the period 1999–2010, with a 3.7:1 female-to-male ratio. Juvenile DTC has aggressive clinical appearance showing cervical nodal involvement in most of the cases, often associated with distant metastatic disease. Nevertheless, comparing with adults, the overall mortality rate in children is not increased. There is no single published guideline for the management of juvenile DTC. The activity of I-131 may be adjusted by body weight (1.85–7.4 MBq/kg) or by age (1/3 of the adult activity is administered to a 5-year-old; 1/2 of the adult activity in a 10-year-old; and 5/6 of the adult activity in a 15-year-old) or surface area. Radioiodine ablation which is established on different patient body characteristics (weight, surface area, thyroid bed radioiodine uptake) seems to be an adequate strategy to fixed dosing or to flexible dosing based on age. In children, some physicians use fixed activities 1.1–11.0 GBq, while others use I-131 activities adjusted activity to body weight (37.0–92.5 MBq/kg). Dosimetry enables I-131 treatment on a calculated patient-specific basis. In our institution, during the period of January 1977 till December 2012, 1,502 DTC patients were treated with I-131. Among these patients, 53 patients were juvenile (mean age, 16.5 years; range, 7–20 years). We detected recurrent disease in 22% of patients with a median time to recurrence of 52 months. The probability of recurrence was 16.7% at 5 years, 22.3% at 10 years, and 33.3% at 15 and 23 years after the initial treatment. The significant prognostic factors of the recurrent DTC include the type of initial treatment (extent of primary surgery and administration radioiodine treatment), patient's age at diagnosis, and tumor multifocality. There were no adverse effects in subsequent pregnancies - eleven female patients (cumulative activity, 3.7–40 GBq of I-131) subsequently had children; complete remission was achieved in 9, partial remission was achieved in 1, and disease related death occurred in 1. Conclusion: With aim to reduce the rate of relapse and improve follow-up of recurrent DTC, total thyroidectomy followed by RAI seems to be the most beneficial initial treatment for patients with

juvenile DTC. The use of RAI is safe, without adverse effects on subsequent fertility or secondary malignancy.

## **How a technologist need to be prepared for a congress**

**C. Pestean, Cluj Napoka**

There is a still growing interest or nuclear medicine technologists to actively participate or initiate research projects and consequently to publish and present their scientific work.

To present a scientific paper is only the final step of a research process. For this, the researchers need to know the context in which they are starting the research, to be aware of the possibilities to disseminate the information, and, to be efficient, to know all those facilities that can make their work easier and more professional.

In this purpose are useful and even mandatory electronic databases of articles and journals which offer the necessary information to establish the context in which the research is starting, but also to help in gathering the bibliographic data. MEDLINE is such a database offering over 22 millions of scientific articles aiming biomedical sciences. The articles which are MEDLINE indexed can be easily reached using PubMed, a research engine. The research must be relevant and valid. To publish the research results could be a real challenge. Very useful are some electronic facilities that come to help the authors. The electronic libraries like Zotero, Mendeley, EndNote are extremely useful for the authors to more easily and accurately to manage the bibliographic references. The presentation of the results in a scientific session of a congress needs to be performed in a professional way, respecting the recommendation given by the scientific committee and needs to transfer to the audience the appropriate message giving all the details related to the research. In this way, the purpose of the authors will be accomplished: to share the results of their research with the professional community in their field of work.

## **PET/CT methodology and priciples: instrumentation, protocols, calibration**

**C. Pestean, Cluj Napoka**

Hybrid nuclear imaging is a challenging specialty requesting that those professionals involved in daily practice to have consistent knowledge regarding the scanning devises, the working protocols using different radiopharmaceuticals in different pathologies and also about how to maintain the scanner and other instrumentation in the best condition respecting all the quality control and quality assesment standards.

The scannerThe PET/CT scanner combine two different imaging methods, bringing together two perspectives for the fused image: the morphological

perspective given by the reconstruction of CT acquired data and the functional perspective offered by the PET image using the assessments of different physiopathological processes based on the use of the appropriate radiopharmaceutical. Highly specialization is needed for technologists using these devices.

Dedicated protocols in different pathologies using different radiopharmaceuticals are developed and designed to obtain an accurate and as much as possible standardized image, aspects that are mandatory in a medical field where developments and changes occur tremendously. These protocols need to be known by nuclear medicine technologists involved in hybrid diagnostic procedures with all the aspects related to patient preparation, scanning parameters, patient management, possible sources of errors that may bias the image.

To ensure the quality of the image it is necessary to ensure the quality of the equipment. Calibration procedures are aimed to keep the instrumentation to work in the parameters established by the manufacturer. It is in the duty of the nuclear medicine technologists to know these procedures and, depending on the job profile, to be able to perform these procedures, being directly responsible of the image quality.

## **PET/CT methodology and principles: image acquisition, image correction, image reconstruction**

**C. Pestean, Cluj Napoca**

Beyond the instrumentation, the patients and the staff, there are other steps until the acquired data to become medical image. In these steps the acquired data is corrected and reconstructed into the well-known by now the PET/CT image.

There are some aspects which are depending only by the instrumentation, like some technical aspects of image correction and image reconstruction but also some aspects are depending very much on the nuclear medicine technologist manipulating the scanner. Therefore it is highly demanded that the personnel to be aware of all the aspects related to image acquisition, correction and reconstruction. In this way, the principle of the examination method is fully understood and the main premise for a quality examination is met.

The theoretical and practical details regarding the acquisition, correction and reconstruction will thus represent the main topics of any training which is necessary to be completed before to start working in hybrid PET/CT imaging and even at an advanced level.

## **SPECT/CT Imaging: instrumentation Development**

**S. Rep, L. Ležaić**

**Department for Nuclear Medicine,  
University Medical Centre Ljubljana**

Single photon emission computed tomography (SPECT) systems are used to image accumulation and distribution of radiopharmaceuticals to provide physiological information for diagnostic and therapeutic purposes. In the past several years SPECT have produced new developments in hardware technology and image processing algorithms. There have been improvements in scintillators, photon transducers and greater availability of semiconductor technology. New clinical devices include more sensitivity cardiac SPECT systems that improve image quality and reduce acquisition time. The progress in processing algorithms provide substantial reductions in SPECT acquisition time without sacrificing diagnostic quality.

## **Parathyroid Imaging**

**S. Rep, L. Ležaić**

**Department for Nuclear Medicine,  
University Medical Centre Ljubljana,**

Parathyroid scintigraphy, based on the accumulation and distribution of radiopharmaceutical, usually  $^{99m}\text{Tc}$ -MIBI. Most centers used for the diagnosis of parathyroid adenomas dual-phase, subtraction scintigraphy, SPECT or SPECT/CT. The disadvantage of these methods is a poor image resolution and sensitivity of the imaging systems. Some PET tracers may be clinically useful to image parathyroid adenomas with advantage of superior image resolution and high-count sensitivity of imaging systems. The aim of presentation is define the diagnostic value of PET/CT  $^{18}\text{F}$ -choline in compare to  $^{99m}\text{Tc}$ -MIBI. Determine the optimal imaging time for  $^{18}\text{F}$ -choline PET/CT and describe advantages of  $^{18}\text{F}$ -choline PET/CT in comparison to the SPECT/CT and subtraction scintigraphy.

## **CLINICAL PROTOCOL OF SPECT-CT BONE SCAN**

**Jovanovska A, Dimcheva M, Sergieva S**

**Department of Nuclear Medicine, Sofia Cancer Center, Sofia**

**INTRODUCTION:** Planar images of bone scan is one of the most frequent in vivo procedures for investigation of bone metastases in the field of nuclear medicine. Visualizing bone metabolism, it shows a relatively high sensitivity to detect skeletal lesions, but has limitations in terms of specificity and spatial resolution, even when single-photon emission computed tomography (SPECT) is used. Combining SPECT with X-ray computed tomography helps overcome these limitations. In this work, we provide the details for the acquisition, processing, and display of the planar and the fused SPECT-CT images of bone scan, with a dual-head SPECT-CT gamma camera SymbiaT2, Siemens. **METHODS:** Bone scan imaging were acquired after intravenous administration of 740 MBq Tc-99m MDP. Planar whole body bone acquisition was performed with scan speed 17cm/min, matrix 256x1024. SPECT acquisition was step and shoot, and the following parameters were used: angular range 180 degrees, 256 x 256 matrix, 120 total steps and large field of view 64 views. Low-dose CT scans were acquired with the following parameters: 130 kVp, 30 mA, 0.8 s/gantry rotation, 256 x 256 matrix, and 5 mm slice thickness. **RESULTS:** The superiority of SPECT/CT over planar whole body bone scan has been clearly demonstrated for the imaging of benign and malignant diseases of patients who underwent bone scan in our department. **CONCLUSION:** SPECT-CT considerably reduces the number of false positive and false negative results in patients with cancer, which is essential for conduction of their optimum treatment.

## **THYROID & EXTRATHYROID MALIGNANCIES**

**Ugrinska A**

**University "Ss Cyril and Methodius", Medical Faculty, Institute of Pathophysiology and Nuclear Medicine "A. Isak S Tadzer", Skopje**

Thyroid hormones play an important role in the cellular metabolism, proliferation and differentiation. Therefore their role has been implied in several types of malignancies, but most of the studies focus on hormone sensitive malignancies, especially the breast cancer. The issue is very important from clinical stand-point having in mind that thyroid disorders are very frequent in female population. However the research till now has yielded controversial results. The available data from the epidemiologic studies showed in some studies clear correlation of hyperthyroidism and breast cancer, higher pre-morbidity levels of T3 in breast cancer but also there are studies that did not found any link between thyroid function and breast cancer. The issue of thyroid autoimmunity was also raised in the previous decade showing association between different types of thyroid antibodies and these malignancies. Also the role of iodine has been studied. Iodine, in addition to its incorporation into thyroid hormones, is bound into antiproliferative iodolipids in the thyroid called iodolactones, which may also play a role in the proliferative control of mammary gland. Epidemiologic studies showed lower incidence of breast cancer in countries with high iodine intake. The research in this field continues and may generate sufficient data to be incorporated in the screening recommendations for breast cancer in particular groups of women and for the screening for thyroid disorders in patients with breast cancer. Also research is concentrated on the therapeutic possibilities of iodine, radioiodine and T3 in this group of patients.



## **Management of low-risk thyroid cancer**

John T. Koutsikos, MD, PhD

Nuclear Medicine physician, Nuclear Medicine Dept., 401 General Military  
Hospital, Athens

Thyroid cancer is the most common endocrine malignancy. Worldwide, its incidence has increased substantially over the past 50 years. More cases of thyroid cancer are found every year than all leukemias and cancers of the liver, pancreas, and stomach. Most of these incident cases are papillary in origin and are both small and localized. Although surgery is traditionally viewed as the cornerstone treatment for these tumors, there is less agreement about the extent of surgery (lobectomy vs. near total thyroidectomy) and whether prophylactic central neck dissection for removal of lymph nodes is needed.

It is also unclear whether the administration of radioiodine provides any benefit in low-risk cases after a complete surgical resection, and radioiodine is not recommended in patients with disease that is categorized as consisting of a tumor less than 1 cm in diameter and clinical stage N0. Therefore, radioiodine should be used with great care to minimize harm, administer the minimal amount of radioactivity, and involve the best tolerated methods. The use of recombinant human thyrotropin and low-dose (1.1 GBq) postoperative radioiodine ablation may be sufficient for the management of low-risk thyroid cancer.

Zehra Ozcan, MD, FEBNM,

Ege University School of Medicine

Department of Nuclear Medicine

35100 Bornova, Izmir

The most common indications of scintigraphic studies in pediatric gastroenterology include evaluation of gastroesophageal reflux (GER) and gastric emptying (GE) rate, Meckels' diverticulum and extended jaundice of the neonate. The other indications which are less frequently utilized are the assessment of colonic transit rate, protein losing enteropathy and inflammatory bowel diseases. This review will summarize the most common radionuclide studies in pediatric gastrointestinal disorders.

### *Gastroesophageal reflux and gastric emptying rate*

GER, defined as the retrograde passage of the gastric contents into the esophagus is a physiologic event in the young babies. It is often asymptomatic and decreases with age. However, if presence of GER results in the occurrence of nutritional, gastrointestinal or respiratory symptoms, then it is defined as GER disease (GERD). Tc-99m sulphur colloid (SC) labelled milk scan is a common simple procedure for the assessment of GER and provides assessment of GE rate at the same session. The study is performed at the usual feeding time with the usual volume of milk or formula. The children are placed in the supine position, 10-30 sec dynamic frames of 64 matrix were recorded for a total of at least 1 hr by using a low-energy general purpose collimator. Interpretation of the images requires attention to any contamination during feeding or due to possible vomiting. This might result in false positive readings for pulmonary aspiration. Inspection of images on cine-mode is often useful to detect patient movement and retrograde flow of the gastric activity.

Estimation of gastric emptying rate is another advantage of pediatric GER studies. It can be easily calculated by drawing ROI over the stomach avoiding intestinal activity. It can be defined either as  $t_{1/2}$  or residual gastric activity at 60 or 120 min. Gastric emptying rate is

affected by the type of the test meal (liquid or solid), volume and the caloric content and the age of the patient. While actually no data from normal control group is currently available, Siebert et al have found normal gastric emptying rate as 48 % ( $\pm 16$  %) and 51 % ( $\pm 7$  %) at 1 hr in infants and children respectively.

### *Pulmonary aspiration*

Respiratory problems are frequent in children with GER particularly those with neurodegenerative diseases. It is thought that aspiration of saliva, food or gastric contents may cause severe pneumonitis or bronchopneumonitis. Pulmonary aspiration can be detected by usual Tc-99m SC labeled milk scan, however it has low detection rate. In order to improve the detection rate, the technique has been modified and defined as "salivagram". Salivagram is a simple and physiologic method performed by administering a small volume (usually < 100  $\mu$ l) of Tc-99m SC labeled liquid onto the tongue. After allowing it to mix with the oral secretions, sequential images are taken during a 60 min period in the supine position. Tracer accumulation in the tracheobronchial tree or lung parenchyma support pulmonary aspiration.

### *Meckel's diverticulum*

Meckel's diverticulum is a common congenital abnormality of the gastrointestinal tract. It is an embryogenic remnant of the omphomesenteric duct. The most common clinical presentations are bleeding which is mostly painless, intestinal obstruction and inflammatory complications.

Tc-99m pertechnetate is administered usually with a dose of 3.7 MBq/kg. Dynamic images at a flow rate 1 sec for the first 60 sec are taken initially to detect any vascular malformation, or bleeding focus and then the imaging period is continued for 30 min. Delayed images may at 1-2 hr may be recorded in cases with negative findings. Acquisition of lateral images is useful to discriminate renal pelvic activity that may cause misinterpretation. The anterior location of the meckel diverticulum can also be demonstrated by SPECT or SPECT/CT when available. Several drugs, histamine blockers, pentagastrin or glucagon may be used to enhance the detection rate. False-positive results may be due to gastrogenic cysts, intestinal duplications, inflammatory bowel disease, obstruction and neoplasms.

### *Biliary atresia*

Biliary atresia is a congenital disease of unknown etiology in which prenatal biliary inflammation leads to fibrosis and atresia. It typically presents by the age of 1 month with persistent jaundice. The location and the type of the atretic biliary tree is usually variable. Hepatobiliary scintigraphy is around 91 % accurate with 97 % sensitivity and 82 % specificity for the detection of biliary atresia. Normal uptake and excretion of Tc-99m IDA in a jaundiced neonate excludes the diagnosis of biliary atresia. Phenobarbital administration prior to imaging improves the accuracy by inducing hepatic enzymes.

### *Suggested reading:*

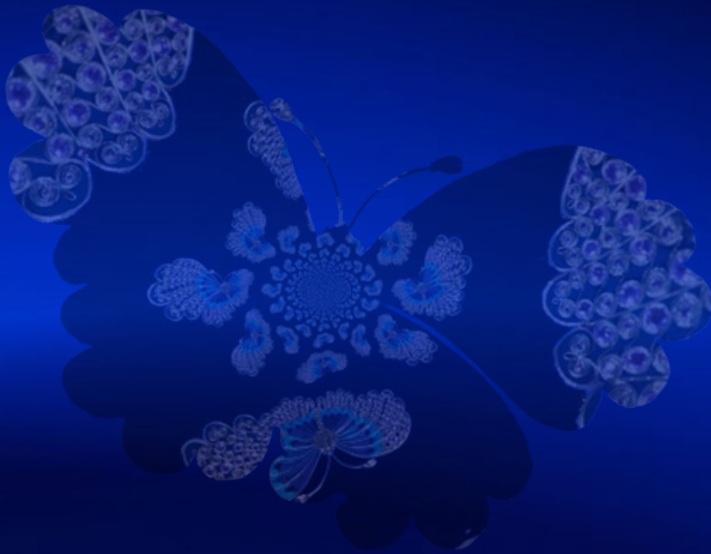
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# ORAL PRESENTATION

## DIAGNOSTIC PERFORMANCE OF IAEA SOFTWARE PACKAGE FOR THE ANALYSIS OF RENAL DYNAMIC SCINTIGRAPHY: THE VALUES OF QUANTITATIVE PARAMETERS OF Tc-99m MAG3 RENOGRAPHY IN HEALTHY INDIVIDUALS

Beatović S<sup>1</sup>, Jakšić E<sup>1</sup>, Janković M<sup>2</sup>, Antić V<sup>3</sup>, Blagić M<sup>3</sup>, Šobić-Šaranović D<sup>1</sup>, Artiko V<sup>1</sup>

1. University of Belgrade, Faculty of Medicine, Center for Nuclear Medicine, Clinical Center of Serbia
2. University of Belgrade, Faculty of Electrical Engineering
3. Center for Nuclear Medicine, Clinical Center of Serbia Belgrade

**Objectives** of this study were to implement the International Atomic Energy Agency (IAEA) Software Package into analysis of Tc-99mMAG<sub>3</sub> dynamic scintigraphy and to validate the results of renogram parameters by comparing with their reference values established by consensus reports.

**Patients and Methods:** Study population consisted of 52 healthy subjects in age range 43 to 64 years who were evaluated by dynamic scintigraphy for kidney donation. IAEA software was applied to process the studies. Parameters analyzed were: time to maximum activity ( $T_{max}$ ), time to half maximum ( $T_{1/2}$ ) of renogram, normalized residual activity at 20 minutes ( $NORA_{20}$ ), output efficiency at 20 minutes ( $OE_{20}$ ), whole kidney mean transit time (MTT) and mean parenchymal transit time (MPTT).

**Results** were presented as follows:  $T_{max}$ :  $3.4 \pm 0.7$  min;  $T_{1/2}$ :  $6.1 \pm 1.5$  min;  $NORA_{20}$ :  $0.34 \pm 0.09$ ;  $OE_{20}$ :  $93 \pm 2.2\%$ ; MTT:  $2.2 \pm 0.4$  min and MPTT:  $1.7 \pm 0.4$  min. Relative function for left and right kidney was 52% and  $48\% \pm 2.4\%$ , respectively. Excellent agreement was observed between obtained values of renogram parameters and their reference values. Significant linear correlation between  $NORA_{20}/OE_{20}$  was obtained ( $r = -0.936, p < 0.01$ ).

**Conclusion:** IAEA Software gives reliable values of numerical parameters of kidney transit. Results obtained for normal kidneys were almost identical with previously reported reference values for MAG<sub>3</sub> parameters.  $NORA_{20}$  highly corresponds with  $OE_{20}$  and could replace the former parameter in evaluation of kidney drainage. The preliminary results support widespread use of IAEA software in order to standardize technique of dynamic renal scintigraphy.

## ROLE OF RENAL OUTPUT EFFICIENCY AND NORMALIZED RESIDUAL ACTIVITY IN PREDICTING KIDNEY OUTFLOW OBSTRUCTION IN CHILDREN WITH ANTENATALLY DETECTED HYDRONEPHROSIS

Beatović S<sup>1</sup>, Jakšić E<sup>1</sup>, Janković M<sup>2</sup>, Radulović M<sup>3</sup>, Šobić-Šaranović D<sup>1</sup>, Artiko V<sup>1</sup>.

1. University of Belgrade, Faculty of Medicine, Center for Nuclear Medicine, Clinical Center of Serbia
2. University of Belgrade, Faculty of Electrical Engineering
3. Military Medical Academy, Belgrade

**Objectives** of this study were to assess diagnostic utility of renal output efficiency (OE) and normalized residual activity (NORA) in quantifying diuretic response in children with hydronephrosis HN and to determine whether these parameters can differentiate between hypotonic unobstructed kidneys and severely obstructed kidneys.

**Patients and methods:** 50 children with HN (median age 16 months) were investigated with MAG<sub>3</sub> renography. 22-minutes acquisition with 132 10-sec images was applied. Furosemide was administered at second minute (F+2). Post-void image was acquired at 60 minute. Two observers analyzed each study and classified kidneys into three categories. Group 1: 42 kidneys contralateral to hydronephrotic kidney, without structural abnormalities; group 2: 49 non-obstructed kidneys; group 3: 8 obstructed kidneys. Parameters analyzed were: NORA at 20 minute (NORA<sub>20</sub>), OE at 20 minute (OE<sub>20</sub>) and post-micturition NORA (NORA PM).

**Results:** Normal kidneys presented with: NORA<sub>20</sub> ≤ 0.4, OE<sub>20</sub> ≥ 90% and NORA PM ≤ 0.05. Results (mean ± SD) for group 2 were: NORA<sub>20</sub>: 0.6 ± 0.2; OE<sub>20</sub>: 87 ± 7.8%; NORA PM: 0.03 ± 0.02. For group 3: NORA<sub>20</sub>: 2.2 ± 0.3; OE<sub>20</sub>: 57 ± 9.6%; NORA PM: 0.27 ± 0.13. Significant differences between group 2 and 3 for all parameters were seen (p < 0.001). Significant inverse linear correlation between NORA<sub>20</sub> and ROE<sub>20</sub> was obtained (R = - 0.982). ROC analysis revealed cutoff values for obstruction at 1.62, 71% and 0.11 for NORA<sub>20</sub>, OE<sub>20</sub> and NORA PM, respectively.

**Conclusion:** OE<sub>20</sub>, NORA<sub>20</sub> and NORA PM are highly sensitive and specific parameters of renal excretion. They help in differentiating between obstruction and non-obstructive dilatation and improve diagnostic accuracy of diuretic renography in children with HN.

## **Localization of an insulinoma with $^{99m}\text{Tc}$ -HYNIC-exendin-4 in a patient with situs inversus: a case report**

**Luka Lezaic MD PhD<sup>1</sup>, Petra Kolenc Peitl MPharm PhD<sup>1</sup>, Katja Zaletel MD PhD<sup>1</sup>, Iztok Stotl MD<sup>2</sup>, Ales Tomazic MD PhD<sup>3</sup>, Anna Sowa-Staszczak MD<sup>4</sup>, Renata Mikolajczak<sup>5</sup> and Alicja Hubalewska-Dydejczyk MD PhD<sup>4</sup>**

<sup>1</sup>Department for Nuclear Medicine, University Medical Centre Ljubljana

<sup>2</sup>Department of Endocrinology, Diabetes and Metabolic Diseases, University Medical Centre Ljubljana

<sup>3</sup>Department for Abdominal Surgery, University Medical Centre Ljubljana

<sup>4</sup>Nuclear Medicine Unit, Department of Endocrinology, Jagiellonian University Medical School, Cracow

<sup>5</sup>National Centre for Nuclear Research Radioisotope Centre POLATOM, Otwock

### **Introduction**

Insulinomas are rare neuroendocrine tumours with characteristic clinical and biochemical features. Cure is achieved by surgical excision, which requires preoperative localization of the tumour. This is frequently difficult due to their small size. Sensitivity of conventional imaging methods combined approaches 80%; GLP-1 receptor scintigraphy is a novel imaging technique that localizes insulinomas with high accuracy.

### **Case description**

A 51-year old female with complete situs inversus was admitted to the Department of endocrinology, diabetes and metabolic diseases due to recurrent hypoglycemia. After the fast test, insulinoma was suspected as the possible cause. Contrast-enhanced CT (CECT) scan showed a small hypervascular lesion in the pancreas. Endoscopic ultrasound (EUS) was inconclusive due to difficult orientation. Somatostatin receptor scan (SRS) was negative.

A GLP-1 receptor SPECT/CT scan was performed to confirm the tumour location, showing a lesion at the junction of the body and tail of the pancreas. At operation the following day, a small tumour was found and removed at the site indicated by GLP-1 receptor scan and later histologically confirmed.

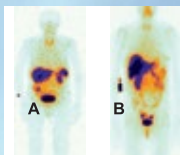
### **Conclusion**

Complete situs inversus in the patient additionally complicated an already difficult localization of an insulinoma. GLP-1 receptor scintigraphy provided accurate lesion localization and allowed for adequate planning of the surgical procedure.



# Tektrotyd

## SPECT Imaging of SOMATOSTATION receptors



Whole body scintigrams of patients  
with suspicion of neoplastic process  
A - Susp. of carcinoid lesion in right iliac region  
B - Pelvic lesions, prob. metastatic

**S**pecificity  
**P**recision  
**E**fficiency  
**C**onvenience  
**T**c-99m labelling

**$^{90}\text{Y}$ -ItraPol,  $^{177}\text{Lu}$ -LutaPol**  
for radiolabelling of radiotherapeutic  
targeting agents



Hot boxes for LutaPol  
and ItraPol production

National Centre for Nuclear Research, Radioisotope Centre POLATOM  
Andrzej Sołtan 7, 05-400 Otwock, Poland  
Phone: + 48 22 2731840, fax: + 48 22 779733, [polatom@polatom.pl](mailto:polatom@polatom.pl) e-mail: [polatom@polatom.pl](mailto:polatom@polatom.pl)



BIOMEDICAL  
IMAGING AND  
THERAPY FOR  
PERSONALIZED  
HEALTHCARE

## ONE DECADE OF GAMMAKEY SYSTEM – IMPORTANCE OF NON-STANDARD FEATURES IN CLINICAL NUCLEAR MEDICINE

Janković M<sup>1</sup>, Koljević Marković A<sup>2</sup>, Beatović S<sup>3,4</sup>, Todorović-Tirnanić M<sup>3,4</sup>, Odalović S<sup>3</sup>, Antić V<sup>3</sup>, Petrović N<sup>3,4</sup>, Artiko V<sup>3,4</sup>, Popović D<sup>1</sup>

<sup>1</sup>University of Belgrade - Faculty of Electrical Engineering, <sup>2</sup>National Cancer Research Center, <sup>3</sup>Center for Nuclear Medicine, Clinical Center of Serbia,

<sup>4</sup>University of Belgrade - Faculty of Medicine, Belgrade

**Objectives:** Research in nuclear medical imaging imposes defining new parameters and adding new computer-aided diagnosis (CAD) algorithms that could not be found in commercial dedicated clinical software. The aim of this paper is to present the application of non-standard features in dynamic and multi-day static scintigraphy that we have realized either as third party applications or as options of our home-made GammaKey system, used in daily clinical practice and research in Serbia from 2005.

**Methods:** The following analyzes were evaluated: 1) testing of splenectomy efficacy in the case of thrombocytopenia with normal production (based on estimation of indices of platelet sequestration, production and survival time from multi-day static scintigraphic studies), 2) *Submarine* processing for localization and visualization of small parathyroid adenomas in patients with concomitant thyroid disease using dual tracer dynamic scintigraphy, 3) automatic calculation of commonly investigated quantitative salivary and oral indices for objective assessment the stage of Sjögren's syndrome (maximum accumulation, maximum secretion, secretion velocity, uptake ratio, parotid : submandibular ratio, ejection fraction, pre-stimulatory and post-stimulatory oral activity).

**Results:** We illustrated the advantages and clinical significance of using home-made interfaces through examples of clinical studies.

**Conclusion:** All presented features improve and facilitate daily clinical practice and research. Implementation of non-standard features as third party applications or open source software has a positive effect on the research, especially in developing countries. The use of such applications is particularly important in multi-center studies where standardization in processing and defining reference is a necessary condition for the validity of joint results.

## QUANTIFICATION OF SMALL SIZE LESIONS IN DYNAMIC SCINTIGRAPHY APPLIED IN PARATHYROID LESIONS: AN ADDITIONAL PREDICTIVE VALUE FOR DIFFERENTIAL DIAGNOSIS VS. THYROID NODULAR DISEASE

Koljevic Markovic<sup>1</sup>, M. Jankovic, G. PupiĆ“R. Džodić<sup>1</sup>National Cancer Research Center, Belgrade, <sup>2</sup>Faculty of Electrical Engineering, University of Belgrade, Belgrade, <sup>3</sup>Faculty of Medicine, University of Belgrade

**Aim:** Aiming to improve specificity of parathyroid scintigraphy in concomitant thyroid nodular disease, we developed a new processing method in ROI time/activity data analysis.

**MM:** Total of 53 patients, median age of 57 years, diagnosed as hyperparathyroidism (PHPT) and ultrasound report of nodular goiter, underwent preoperative, dual- tracer: 99m Tc-pertecnetat and 99mTc-MIBI, double- phase scintigraphy by EANM guidelines (2009).Specially designed software we developed examined ROI time/activity changes in the form of grid with optional sizes. We correlated our findings with parathormone (PTH) levels, histology and conventional scintigraphic findings.

**Results:** PTH was increased in the group: median 120,2 pg/ml (range 70-658pg/ml).Following histopathology: a) thyroid - benign: adenoma: 45(83%)pts; malignancy: 8 (10%)pts, b) parathyroid – autonomy (PTA) 53(70,2%):. solitary: 44 patients, hyperplasia: 8 pts- 7/8 patients with two lesion and 1/7 had all four lesions and one PT carcinoma;.c.) median PTA volume was 760(55-6125)mm<sup>3</sup>.

Standard findings (subtraction, oblique planar scans and delayed phase) in total of 63 lesion (in 53 pts) had 10 FN (mostly in hypeplasia PTA), and PPV was 81%.

Thyroid TACs represented, as expected, exponentially declining curves but parathyroid lesions had typical uptake pattern in the form of late phase peak, independent to PTA volume and/or PTH levels. The thyroid gland washout was up to 28% in normal, adenoma or thyroid carcinoma tissue. A new processing method for PTA had PPV 97%.

**Conclusion:** Application of new imaging data quantification, was effective in small parathyroid lesions concomitant to thyroid nodular disease, complementary used with standard protocols.

## FDG PET IN PRESURGICAL EVALUATION OF FOCAL EPILEPSY

L. Brajković<sup>1</sup>, D. Sokić<sup>2</sup>, N. Vojvodić<sup>2</sup>, A. Ristić<sup>2</sup>, S. Janković<sup>2</sup>, D. Šobić-Šaranović<sup>1</sup>, V. Artiko<sup>1</sup>

Center for Nuclear Medicine<sup>1</sup>, Clinical Center of Serbia

Clinic for Neurology<sup>2</sup>, Clinical Center of Serbia, Belgrade, Serbia

lelabrajko62@gmail.com

Multimodal imaging could provide information about the relationships between the epileptic lesion (structural MRI), irritative zone (interictal EEG), ictal onset zone ( ictal EEG, ictal perfusion SPECT, ictal FDG- PET), functional deficit zone (interictal FDG-PET), eloquent cortex (functional MRI) and improve noninvasive presurgical evaluation of patients with intractable focal epilepsy.

**Aim:** To evaluate usefulness of functional imaging FDG-PET in presurgical lateralization and localization of epileptic foci.

**Materials and methods:** We performed FDG-PET in 205 patients (age 5-65) with temporal and extratemporal focal pharmacoresistant epilepsy. The images were evaluated by visual analyses and findings were compared with the epileptogenic zone determined by scalp video EEG monitoring and MRI results.

**Results:** Interictal FDG-PET has shown regions of hypometabolism in: temporal lobe unilaterally in 121 patients, bilaterally in 11 patients, frontal lobe 35 patients, parietal lobe 11 patients, frontoparietal 2, multifocal zones of hypometabolism in 11. In 7 patients we performed ictal PET (2 patients with nonconvulsive status epilepticus, 1 with epilepsy partialis continua, 4 with complex partial seizure) –epileptogenic zones were visualised as hypermetabolic regions. We detected epileptogenic zone in 187 patients (91%) with FDG -PET.

**Conclusion:** FDG- PET neuroimaging method allows visualization of the epileptic focus as hypometabolic region at the interictal PET and hypermetabolic region at the ictal PET. PET is important in the presurgical evaluation of patients with pharmacoresistant focal epilepsy, especially if MRI is normal or MRI and video EEG results are discordant.

FIRST POLISH EXPERIENCES IN THE CYCLOTRON PRODUCTION OF <sup>99m</sup>Tc

Pawlak D, Wojdowska W, Parus J, Cieszykowska I, Janiak T, Jerzyk K, Mielcarski M, Barcikowski T, Garnuszek P, Mikołajczak R.

National Centre for Nuclear Research, Radioisotope Centre POLATOM, Otwock

### *Aim*

The <sup>99m</sup>Tc worldwide needs are practically covered nowadays by its production from fission of <sup>235</sup>U. Due to aging of nuclear reactors delivering it on one hand

and the necessity to use low enriched uranium on the other, alternative methods of  $^{99m}\text{Tc}$  production are being developed. Our goal was to develop technology suitable for  $^{99m}\text{Tc}$  production in a medical, 16 MeV cyclotron, and its further separation.

#### *Materials and methods*

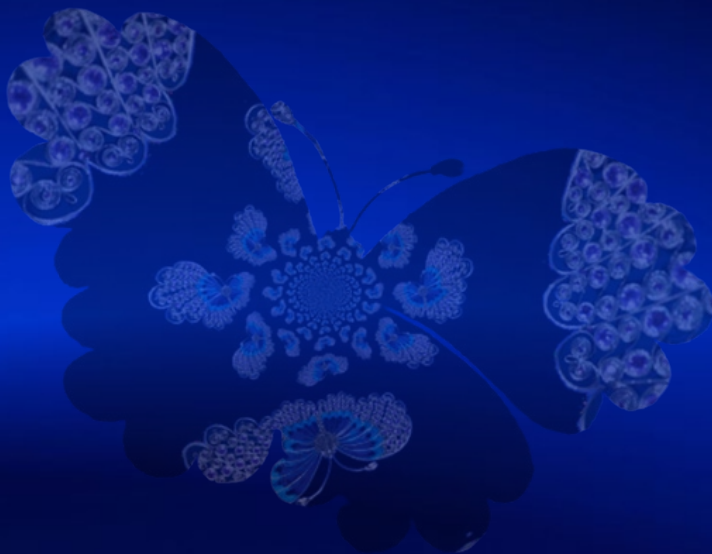
Molybdenum target was prepared by pressing metal powder containing 99.8% of  $^{100}\text{Mo}$ . After sintering in hydrogen atmosphere at  $1800^{\circ}\text{C}$  for 60 min, the pellet was loaded into aluminum holder which was mounted in GE PETtrace 840 cyclotron (at HIL, University of Warsaw) proton beam and irradiated for 2 h at 2  $\mu\text{A}$  current to total activity of 1.6 GBq at the EOB.

#### *Results and discussion*

The target was dissolved in 30%  $\text{H}_2\text{O}_2$  and alkalized with 10M NaOH.  $^{99m}\text{Tc}$  was separated in 3 columns connected in series containing AnaLig, Dionex and alumina beds. The  $^{99m}\text{Tc}$  recovery yields amounted to 76.3%. The  $^{99m}\text{Tc}$  solution was free of molybdenum. Method is further optimized to increase separation yield.

#### *Acknowledgments*

We are thankful to the staff of the Heavy Ion Laboratory of the University of Warsaw for target irradiation. This work was supported by the National Centre for Research and Development within the Applied Science Program NCBiR Nr PBS1/A9/2/2012 and by the IAEA CRP contract 17419.



# POSTER PRESENTATION

**FIRST POLISH EXPERIENCES IN THE CYCLOTRON PRODUCTION OF  $^{99m}\text{Tc}$**   
**Pawlak D, Wojdowska W, Parus J, Cieszykowska I, Janiak T, Jerzyk K,**  
**Mielcarski M, Barcikowski T, Garnuszek P, Mikołajczak R.**  
**National Centre for Nuclear Research, Radioisotope Centre POLATOM,**  
**Otwock**

*Aim*

The  $^{99m}\text{Tc}$  worldwide needs are practically covered nowadays by its production from fission of  $^{235}\text{U}$ . Due to aging of nuclear reactors delivering it on one hand and the necessity to use low enriched uranium on the other, alternative methods of  $^{99m}\text{Tc}$  production are being developed. Our goal was to develop technology suitable for  $^{99m}\text{Tc}$  production in a medical, 16 MeV cyclotron, and its further separation.

*Materials and methods*

Molybdenum target was prepared by pressing metal powder containing 99.8% of  $^{100}\text{Mo}$ . After sintering in hydrogen atmosphere at  $1800^{\circ}\text{C}$  for 60 min, the pellet was loaded into aluminum holder which was mounted in GE PETtrace 840 cyclotron (at HIL, University of Warsaw) proton beam and irradiated for 2 h at 2  $\mu\text{A}$  current to total activity of 1.6 GBq at the EOB.

*Results and discussion*

The target was dissolved in 30%  $\text{H}_2\text{O}_2$  and alkalized with 10M NaOH.  $^{99m}\text{Tc}$  was separated in 3 columns connected in series containing AnaLig, Dionex and alumina beds. The  $^{99m}\text{Tc}$  recovery yields amounted to 76.3%. The  $^{99m}\text{Tc}$  solution was free of molybdenum. Method is further optimized to increase separation yield.

*Acknowledgments*

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## **$^{99}\text{Mo}$ / $^{99\text{m}}\text{Tc}$ SHORTAGE: FROM PERSPECTIVE OF NUCLEAR MEDICINE PHYSICIAN**

**Ince S, Alagoz E, Emer O, San H, Okuyucu O, Ayan A, Karacalioglu O, Gunalp B, Arslan N.**

**Gulhane Military Medical Academy and School of Medicine, Department of Nuclear Medicine, Etlik, Ankara**

**Objective:** The current availability of  $^{99\text{m}}\text{Tc}$  is mainly based on  $^{99}\text{Mo}$  generators produced from the fission of  $^{235}\text{U}$  in nuclear reactors using highly enriched uranium targets. There's a growing shortage of  $^{99\text{m}}\text{Tc}$  which is crucial in nuclear medicine imaging in recent years for national policies, technical and economic reasons. The major problem is shutting down of two aging reactors (NRU, Canada and OSIRIS, France) for repair several times recently, which produce most of the  $^{99}\text{Mo}$  used in the world. Other main reactor sources (Holland, Belgium, South Africa and Australia) are unable to maintain ongoing demand. Besides the high cost of construction of a new reactor, existing processing facilities will be unsufficient in near future. Therefore, alternative strategies for production of both  $^{99\text{m}}\text{Tc}$  and  $^{99}\text{Mo}$  are at issue today. Direct Tc-99m production from  $^{100}\text{Mo}$  with accelerator-based technologies doesn't need a reactor which is a promising method. However, this is only useful for local production because of short half life of  $^{99\text{m}}\text{Tc}$ . The aim of this study is to investigate whether lack of these isotopes has impacted end users' practice or facility.

**Methods:** We investigated how the problem affects end users and how conscious they are about  $^{99}\text{Mo}$  shortage with a poll performed in Turkish Society of Nuclear Medicine (TSNM) members.

**Results:** All members are aware of the severity of the global  $^{99}\text{Mo}$  shortage in recent years. %90 of the respondents said they had difficulty in providing  $^{99}\text{Mo}$  in their departments. Half of the responses noted they don't have access to a technetium generator source beyond their current supplier. Approximately 8% are operating at less than 50% of their capacity because of the isotope shortage, 30% are operating at 51% to 75% of capacity, and 65% are running at 76% to 100% procedure capacity. In addition, 35% said they had to postpone patient procedures, while 11% noted that procedures were cancelled, 14% used another isotope for the imaging procedure, 14% changed to a different procedure, and 4% of the respondents transferred their patient to another facility. Of the practitioners who changed the procedure, 21% used TI-201 vs. sestamibi, 17% chose F-18 fluoride vs. MDP to perform a bone scan and 12%



opted for a non-nuclear medicine procedure.

**Conclusion:** Mo-99 shortage is a threat that could affect the nuclear medicine industry in the near future. Therefore, new options should be pursued include both reactor and accelerator based strategies to sustain the continued availability of  $^{99m}\text{Tc}$ .

## Evaluation of radiochemical purity and tumor uptake of $^{188}\text{Re}$ -HEDP

T.Tripunoski<sup>1</sup> and D.Mathe,<sup>2</sup> L.Balogh,<sup>2</sup> A.Polyak,<sup>2</sup> A. Ugrinska<sup>1</sup>, Gy. A. Janoki,<sup>2</sup> S. Stojanovski<sup>1</sup>, D. Miladinova<sup>1</sup>, E. Janevik-Ivanovska<sup>3</sup>, O.Vaskova<sup>1</sup>

<sup>1</sup>Institute of Pathophysiology and Nuclear Medicine, Medical Faculty, Skopje

<sup>2</sup>Frederic Joliot-Curie National Institute of Radiobiology and Radiohygiene, Dept. of Applied Radioisotopes, Budapest

<sup>3</sup>Faculty of Medical Sciences, Goce Delcev University, Stip

**Aims.** The aim of the article is to present the preparation, quality control of  $^{188}\text{Re}$ -HEDP and its uptake in spontaneously occurring dog osteosarcomas.

**Materials and methods.** Rhenium [ $^{188}\text{Re}$ ] was obtained from an alumina-based  $^{188}\text{W}/^{188}\text{Re}$  generator (Oak Ridge National Laboratories, USA and MAP Medical, Finland) by elution with 0.9% NaCl solution. The radiopharmaceutical  $^{188}\text{Re}$ -HEDP was prepared by in-house developed HEDP solution.

The radiochemical purity of  $^{188}\text{Re}$ -HEDP was performed by instant thin layer chromatography (ITLC) technique, using ITLC-Silicagel strips developed in 95% acetone.

This study was performed on 14 dogs with spontaneous osteosarcoma receiving an activity between 1.1-2.1 GBq of  $^{188}\text{Re}$ -HEDP. The relative tumor uptake of radiopharmaceutical (T/NT ratio) was calculated by region of interest (ROI) analysis.

**Results.** The radiochemical purity of  $^{188}\text{Re}$ -HEDP showed the labelling yield above 97%.

T/NT ratio of  $^{188}\text{Re}$ -HEDP was ranging between 1.89 to 15.85. On the basis of  $^{188}\text{Re}$ -HEDP tumor uptake, a low, a medium and a high T/NT uptake group of animals was formed with 4-7-3 animals, respectively.

**Conclusions.**  $^{188}\text{Re}$ -HEDP is an attractive alternative bone seeking radiopharmaceutical for palliative treatment of primary as well as secondary metastatic bone lesions.

The use of dogs with spontaneously occurring osteosarcoma as animal model proved to be of high value in the studies of radionuclide therapy as a novel modality of osteosarcoma treatment. Further studies are warranted to investigate the origins of osteosarcoma radiosensitivity as well as radiotoxicity of  $^{188}\text{Re}$ -HEDP.

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**Comparative characteristics of radionuclides Tcm99MIBI and Tcm99TETROFOSMIN in process of biodistribution**  
**Mihajlova S, Risteski LJ, Mihajlova S, Sirvini Z, Sekulovska M**  
**Department of nuclear medicine, Clinical hospital -Bitola**

For diagnostic and localization of myocardial ischemia, the most frequently used radiopreparats in the nucleare medicine department in Clinic Hospital Bitola are Tcm99MIBI and Tcm99TETROFOSMIN.

**The goal** is to perform comparative monitoring of both radionuclides in order to see their performances and obtaining accurate information on global and regional myocardial perfusion scintigraphy. The examination was done intermittently over a period of two years (2010/2011) by using the two radioactive agents, Tcm99MIBI and Tcm99TETROFOSMIN through quantitative analysis of the skenogram detected with SPECT technique.

**Material and Methods**

The examination was conducted on 58 patients (32 man and 26 women) with low likelihood for coronary artery disease on MPS, burdened by the Bruce protocol to sub or maximum level of load and intravenous application of appropriate radioactive dose of Tcm99MIBI or Tcm99TETROFOSMIN. The accumulation of both radiotrasers was estimated in the myocardial wall, divided into 20 segments. For comparative purposes it is defined a segment with maximum accumulation.

**Results**

In a quantitative assessment of the measured impulse segments there were no significant differences between two radionuclides both in rest and stress study, although higher accumulation was detected in Tcm99MIBI radioactive agent. The quantitative analysis of the maximal impulses of Tcm99MIBI and Tcm99TETROFOSMIN in the measured 20 sequences in the region of the left ventricle in rest (47219/44019) and stress (14531/13321), examination showed an approximate accumulation of the average of values without significant importance, which more shows Tcm99MIBI accumulation.

**Conclusion**

The two radiofarmaceutical agents used in this study (Tcm99MIBI i Tcm99TETROFOSMIN) showed similar values in assessing the MPS.

## **Effect of Low Dose CT Attenuation Correction in the Incidence of Ischemia During Myocardial Perfusion Scintigraphy**

**Pipikos T<sup>1</sup>, Vlachou F<sup>1</sup>, Nikaki A<sup>1</sup>, Koletti L<sup>1</sup>, Gogos K<sup>2</sup>, Iakovidou A<sup>1</sup>, Dalianis K<sup>2</sup>, Prassopoulos V<sup>1</sup>;**

**<sup>1</sup>Nuclear Medicine Department Hygeia SA, Athens, Marousi, <sup>2</sup>Medical Physics Department, Hygeia S.A., Athens, Marousi**

**AIM:** Attenuation artifacts can lead to false diagnosis during the interpretation of myocardial perfusion studies. These artifacts can be reduced with the usage of SPECT/low dose CT  $\gamma$ -camera systems. In this study we evaluated the effect of low dose CT based attenuation correction in the performance of myocardial perfusion scintigraphy. **Material and methods:** We compared the findings of attenuation corrected and non attenuation corrected images of 93 patients who underwent myocardial perfusion scintigraphy in the last 2 years and also underwent coronary angiography. Scintigraphy results of ischemia were evaluated as true positive in the patient group with coronary stenosis over 70%. Interpretation of the studies was blinded between corrected and non-corrected images, as well as between scintigraphy and angiography. **RESULTS:** Twenty-six (26) patients had stenosis over 70% in coronary angiography. Both methods identified correctly 24/26 cases. In the group of 67 patients without severe coronary stenosis, there were 25 false positive for ischemia non attenuated scans, while with attenuation correction only 9 false positive scans were found. Sensitivity and specificity for non-attenuated images were respectively: 92% and 62%. For low dose CT attenuated images: 92% and 86%. Sensitivity was high for both image series, but diagnosis was more specific with attenuation corrected images. False positive findings of ischemia were found mainly in the inferior and inferior lateral wall.

**CONCLUSION:** Attenuation corrected images using low dose CT, improves the performance of myocardial perfusion scintigraphy, with less false positive findings.

**The correlation between „gated” single - photon emission computed tomography methoxyisobutylisonitrile early imaging protocol and dobutamin stress echocardiography in patients with ischemic heart disease**  
Bojic L<sup>1</sup>, Sobic – Saranovic D<sup>2</sup>, Petrasinovic Z<sup>3</sup>, Djordjevic Dikic A<sup>3</sup>, Artiko V<sup>2</sup>, Obradovic V<sup>2</sup>

<sup>1</sup>Department of nuclear medicine, Clinical Centre of Montenegro, Podgorica,

<sup>2</sup>Center of nuclear medicine, Clinical Centre of Serbia, Belgrade <sup>3</sup>Clinic for Cardiology, Clinical Center of Serbia, Belgrade

**Introduction:** „Gated” single - photon emission computed tomography methoxyisobutylisonitrile („gated” SPECT MIBI) provides informations about extensivity, severity and reversibility of perfusion abnormalities and global and regional function of left ventricle in patients with known or suspected ischemic heart disease. On the other hand, in recent decades, dobutamine stress echocardiography (DSE) has become one of the most commonly performed non-invasive methods for the evaluation of patients with suspected coronary heart disease, due to the simplicity and safety performance, as well as due to very good sensitivity and specificity for detection of ischemic heart disease.

**Objectives:** To evaluate diagnostic value of early post-stress (ES) „gated” SPECT MIBI protocol and DSE against coronary angiography (CA) as a gold standard for detecting abnormalities consistent with a significant coronary artery stenosis (>70%). Also, we compared ES and DSE findings and we determined a level of agreement between two methods for detection of ischemic heart disease.

**Methods:** The sample included 63 patients with normal or mildly impaired left ventricular function with known or suspected coronary disease. They underwent a 2-day stress-rest „gated SPECT MIBI with the post-stress data acquired at 15 minutes (ES) and 60 minutes (SS) after i.v. injection of 740 MBq of <sup>99m</sup>Tc-MIBI. In all subjects, DSE and CA were performed within 1 month of „gated” SPECT MIBI. The ES and DSE findings were compared against CA to determine their sensitivity/specificity for detecting >70% stenosis. Also, the ES findings were correlated with DSE results in order to assess a level of agreement and diagnostic value these two methods for detection of ischemic heart disease.

**Results:** ES parameters and DSE results show strong correlation, high sensitivity (ES vs. DSE 96% vs. 93%) and specificity (ES vs. DSE: 83% vs. 80%) for detecting >70% coronary stenosis, compared with CA as a gold standard. The difference between two methods was not significant ( $p=1.000$ , McNemar test), with the

unweighted coefficient of agreement ( $\kappa = 0.725$ ) (IP 95%: 0.499-0.952;  $p < 0.001$ ) and with very high percentage of agreement (91%).

**Conclusion:** Both methods, ES „gated” SPECT MIBI and DSE are very sensitive and specific diagnostic tools for detection of ischemic heart disease compared with CA, as a gold standard for detecting abnormalities consistent with a significant coronary artery disease. ES „gated” SPECT MIBI imaging protocol and DSE showed a high level of agreement for detection of ischemic heart disease.

## **Screening for the presence of silent myocardial ischemia using the method of perfusion scintigraphy in diabetic patients**

**Hadžiahmetović M<sup>1</sup>, Kučukalić- Selimović E<sup>1</sup>, Cerić Š<sup>1</sup>, Agić S<sup>1</sup>, Čibo M<sup>2</sup>**

**1. Department of Nuclear medicine, Clinical center University of Sarajevo**

**2. Heart center, Clinical center University of Sarajevo**

**INTRODUCTION:** Coronary heart disease is a late complication of diabetes mellitus and is one of the most common causes of death in more than half of patients with this disease. According to the recommendation of the European and the American Association of Diabetes mellitus, guidelines for the detection of coronary disease in diabetes mellitus, perfusion scintigraphy is one of the leading non-invasive method for the detection of silent myocardial ischemia.

**METHODS:** The study included a total of 80 patients, out of which 40 patients (selective population) with diabetes mellitus who are treated and control the state of progress of the disease. Control group of 40 represents patients who are not suffering from diabetes mellitus already from other diseases which require the same diagnostic procedure.

**RESULTS:** Perfusion scintigraphy was positive in 87.5 % of patients with diabetes mellitus included. The sensitivity of myocardial perfusion scintigraphy (SN) in diabetic patients is 90.3 % and specificity of the test (SP) was 55.6 % compared with coronarography. Coronarographically 38 patients without diabetes mellitus (94.8 %) had positive findings, while the remaining 2 patients with diabetes mellitus (5.2 %) had negative findings.

**CONCLUSION:** The present results indicate that perfusion scintigraphy combined with ergometric test can be used to detect and control patients with silent myocardial ischemia. To check the findings it is necessary to select patients for coronary angiography.

## **The importance of the Myocardial perfusion scan (MPI) in evaluation of patients after Percutaneous Coronary Intervention (PCI)**

**Abdullahu L; Miftari R; Gërqari I; Bajqinca A; Spahiu F; Bajrami I**

**SHSKUK, Clinic for nuclear medicine, Prishtinë**

**SPECT-G-SPM**-has become a routine procedure in nuclear medicine as powerful modality for assessing perfusion and heart function. Very high probability of repeated occlusion of coronary artery after PCI and occlusion of other coronary arteries raises necessitates for early detection and timely intervention.

**Aim** of the study was to determine the role of MPI for early detection of re-occlusion of the arteries after PCI or other deteriorations of coronary arteries. Evaluating and comparing the results obtained from coronarography and SPM.

**Methods:** The study included 28 patients undergoing PCI; from them 20 males and 8 females. In all these patients was made PSM with SPECT-G method (gated) during the exercise and in the rest after I.V. administration of radiopharmaceuticals 99m-Tc-MIBI of 8 MCI (296MBq), respectively 24 MCI (888MBq) with a daily study protocol and were compared with data from coronarography.

**Results:** From the total number of patients undergone coronarography (28), in three of them the result was proved negative for coronary disease and in 25 of them (89%) during coronarography it was found changes in the coronary arteries and were placed stents in order to re-vasculate the affected vessels. The patients who underwent PCI, 7 of them had multivessels intervention (28%), 19 patients were only stent in one of coronary artery (72%), 9 patients in the left descending artery (LAD), 8 patients in right coronary arterie (RCA) and 1 in ramus intermedius (RIM). In 3 patients who had no affected coronary artery during coronarography, also the PSM has resulted with no changes in perfusion. While the patients who had PCI, scintigraphy of myocardial perfusion after placement of stents, has improved in 8 patients, worsened in 9 patients and have had partial improvement in 8 patients.

**Discussion:** In assessing the degree of homogenicity of accumulation of radiopharmacs in the heart muscle during exercise and rest, it was determined a relative degree of abnormality in perfusion of vascular sections and it was evaluated perfusion in all segments those regions. Remaining lesions after placement of stents were assessed for defects in accumulation. This is easier to detect with PSM with 99m Tc-MIBI. Distribution of radio pharmaceuticals in heart is distributed proportionally with circulation of the blood, with the fast



cleansing from blood and slow cleansing from heart muscle. Preparation is simple and there were no adverse effects.

**Conclusion:** According to our data, we have concluded that PSM is an appropriate method for the early detection, identification and monitoring patients with [coronary artery disease](#) (CAD).



Индивидуално дозирање

»» Butterfly Effect ««



## Left ventricular function in acromegaly assessed by radionuclide ventriculography

Zdravkovska M<sup>1</sup>, Pop Gjorcheva D<sup>1</sup>, Pemovska G<sup>2</sup>, Majstorov V<sup>1</sup>, Stojanoski S<sup>1</sup>, Ristevska N<sup>1</sup>, Kochovska Zdraveska M<sup>1</sup>

Institute of Pathophysiology and Nuclear Medicine<sup>1</sup>, Clinic of Endocrinology and metabolism disease<sup>2</sup>, Medical Faculty, UKIM, Skopje

**Background:** to estimate whether the excess of GH and IGF in acromegaly can cause impairment of myocardial systolic and diastolic function and does it depend also on disease duration and activity as well as the age of patients.

**Patients and Method:** LV function at rest was assessed by radionuclide ventriculography in 24 patients (pts), (8 man, 16 female), age 24-63 (mean  $45.6 \pm 12$  y). In all pts the levels of GH, IGF-1 and IGFBP3 were increased as a indicator of an active form of the disease. The 22 healthy controls (2 man, 20 female, age  $44 \pm 17$  y) were examined with the same method.

Pts and controls were divided in two groups, age below and above 40 y to compare the LV systolic (ejection fraction-EF, and peak ejection rate-PER) and diastolic performances (peak filling rate-PFR and PFR/PER ratio) between the groups. We demonstrated that cardiac function (systolic, diastolic) is still preserved in young pts compared to age-matched control group (EF  $64 \pm 3\%$  vs.  $67 \pm 9\%$  (n.s), PER  $-3.27 \pm 0.45$  edv/s vs.  $-3.11 \pm 0.5$  edv/s (n.s.), PFR  $2.98 \pm 0.37$  edv/s vs.  $3.05 \pm 0.4$  edv/s (n.s.), PFR/PER  $0.92 \pm 0.12$  vs.  $0.97 \pm 0.16$  (n.s.). Although the systolic parameter – EF in elderly patients were slightly decreased compared both, to younger pts and controls above 40y (EF  $61 \pm 8\%$  vs.  $64 \pm 3\%$  and EF  $61 \pm 8\%$  vs.  $65 \pm 5\%$ ), including the PER ( $-3.30 \pm 0.65$  edv/s vs.  $-3.27 \pm 0.45$  edv/s and  $-3.30 \pm 0.65$  edv/s vs.  $-3.05 \pm 0.6$  edv/s) the changes were nonsignificant. A significant impairment of LV diastolic filling was observed in elderly pts compared to younger pts (PFR  $2.47 \pm 0.52$  edv/s vs.  $2.98 \pm 0.37$  edv/s,  $p < 0.01$ , PFR/PER  $0.76 \pm 0.15$  vs.  $0.92 \pm 0.12$ ,  $p < 0.0001$ ) and to age-matched controls (PFR  $2.47 \pm 0.52$  edv/s vs.  $3.03 \pm 0.8$  edv/s ( $p < 0.01$ ), PFR/PER  $0.76 \pm 0.15$  vs.  $0.99 \pm 0.18$ ,  $p < 0.001$ )

**Conclusion:** While systolic dysfunction in acromegalic pts at rest is mild and nonsignificant and needs estimation of LV function at peak exercise to be demasced, the significant impairment of myocardial diastolic function as an early presentation of acromegalic cardiomyopathy is present even in basal conditions in elderly pts with long disease duration and activity.

## **ROLE OF FDG-PET IN RENAL CANCER**

**Nikaki A<sup>1</sup>, Kechagias D<sup>1</sup>, Vlachou F<sup>1</sup>, Filippi V<sup>1</sup>, Pipikos T<sup>1</sup>, Savvidou D<sup>1</sup>, Razi E<sup>2</sup>, Gogos K<sup>3</sup>, Merisoglou S<sup>1</sup>, Andreou I<sup>1</sup>, Efthymiadou R<sup>1</sup>, Prassopoulos V<sup>1</sup>;**  
**<sup>1</sup>PET/CT Department ,Hygeia S.A., Athens, Marousi, <sup>2</sup>3rd Oncology Department, Hygeia S.A., Athens, Marousi, <sup>3</sup>Medical Physics Department ,Hygeia S.A., Athens, Marousi**

**Objectives:** to evaluate the usefulness of FDG-PET/CT in restaging renal cancer patients.

**Methods:** 36 examinations (26 patients) were included in this retrospective study. Patients had undergone surgical excision of their primary site, as well as CT and/or MRI (Conventional Imaging:CI) before PET/CT. In 4/36 cases radiotherapy had been applied, in 10/36 cases chemotherapy/targeted therapy. Evaluation of the detected lesions occurred per scan and per organ. Final diagnosis of the lesions was based on follow up, biopsy of the lesion and clinical decision.

**Results:** The commonest histologic subtype was clear cell renal cell carcinoma. 8/36 PET/CT examinations were negative for hypermetabolic lesions. In 28/36 cases PET/CT was positive for at least one hypermetabolic lesion. In 1/28 cases biopsy revealed second primary (lung cancer). Sensitivity of FDG-PET per scan was 90%. Per organ basis, sensitivity of PET in evaluating local disease, abdominal and mediastinal lymph nodes, adrenal glands and osseous disease was  $\geq 90\%$ . FDG-PET had a lower sensitivity for pulmonary lesions, especially small ones; however in one patient with a solitary pulmonary lesion 7mm and negative FDG-PET, the patient was put under surveillance and the lesion did not change during follow up, neither new lesions appeared, therefore it was considered true negative.

**Conclusions:** With respect to the referral bias of our results, this study suggests that PET may have a position in restaging patients with renal cancer after surgical removal of the kidney, particularly in equivocal findings in CI, in evaluation of local recurrence, lymph nodes, adrenal gland and osseous disease.

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## **FDG-PET/CT IN SOLITARY PULMONARY NODULE (SPN) ASSESSMENT**

**Vlachou F<sup>1</sup>, Filippi V<sup>1</sup>, Nikaki A<sup>1</sup>, Savvidou D<sup>1</sup>, Kosmidis P<sup>2</sup>, Iliadis K<sup>3</sup>, Pipikos T<sup>1</sup>, Gogos K<sup>4</sup>, Dalianis K<sup>4</sup>, Andreou I<sup>1</sup>, Efthymiadou R<sup>1</sup>, Prassopoulos V<sup>1</sup>**

**<sup>1</sup>PET/CT Department ,Hygeia S.A., Athens, Marousi, <sup>2</sup>2nd Internal Medicine - Oncology Clinic Hygeia SA, Athens, Marousi, <sup>3</sup>Thoracic Surgery Clinic Hygeia SA, Athens, Marousi, <sup>4</sup>Medical Physics Department ,Hygeia S.A., Athens, Marousi**

**Objectives:** to evaluate the role of FDG-PET/CT in discrimination of malignant/benign solitary pulmonary nodules (SPN), by co-estimating nodule's size and FDG uptake (SUVmax).

**Methods:** 71 patients were enrolled in the study. Nodule's size and SUVmax were co-evaluated. Statistical analysis using un-paired t-test was used for discrimination of lung adenocarcinoma from benign formations such as hamartomas and inflammation, as well as from well-differentiated malignant formations, such as carcinoids. Histologic confirmation was available for all included patients.

**Results:** SUVmax values were statistically significantly higher ( $p < 0.005$ ) for lung adenocarcinomas (average SUVmax  $5.64 \pm 4.6$ ) than the summary of benign/well differentiated carcinoid tumors (average SUVmax  $2.26 \pm 1.14$ ), as well as, separately, than hamartomas (average SUVmax  $1.78 \pm 0.5$ ), carcinoids (average SUVmax  $2.8 \pm 1.5$ ), inflammation (average SUVmax  $\pm 0.98$ ). SUVmax values did not significantly differ between carcinoids, hamartomas and inflammation ( $p > 0.1$ ).

**In a subgroup analysis:**

a) 20 cases, nodule's size  $\leq 1$ cm. There was no statistical significance in SUVmax for differentiation benign from malignant lesions ( $p > 0.05$ ).

b) 36 cases, nodule's size  $> 1 - \leq 2$ cm. There was statistical significance in SUVmax values for differentiation adenocarcinomas from benign/well differentiated carcinoid lesions ( $p = 0.003$ ).

c) 15 cases, nodule's size  $> 2 - \leq 3$ . There was statistical significance in SUVmax values for differentiation adenocarcinomas from benign/well differentiated carcinoid lesions ( $p = 0.0053$ ).

**Conclusion:** PET is a very useful imaging procedure in differentiation of malignant vs benign/well-differentiated carcinoid pulmonary lesions of size  $> 1$ cm. For smaller SPNs, although there is tendency for higher SUVmax values in adenocarcinomas, morphologic characteristics or delayed PET acquisition could be more helpful.

## **Sarcoidosis and 18F-FDG PET/CT imaging - don't miss malignancy**

**Grmek M<sup>\*</sup>, Koren Pucelj N<sup>\*\*</sup>, Tercelj M<sup>\*\*</sup>**

**University Medical Centre Ljubljana, \*Dept. for Nuclear Medicine, \*\*Clinical Dept. for Pulmonary Diseases and Allergy, Ljubljana**

**Aim:** The aim of the article is to present the importance of attentive PET-CT scan readings in patients with sarcoidosis.

**Patients:** In the retrospective study 124 patients (54 male and 70 female) with confirmed sarcoidosis were included. The initial PET-CT investigation was performed between year 2010 and 2013 to establish extent and activity of the disease and in some for the purpose of differential diagnosis or to detect the best site for biopsy. In 60 patients PET-CT investigation was repeated for follow up.

**Methods:** PET-CT investigation - the acquisition on the PET/CT scanner started one hour after injection of the 18F-FDG; activity 4 MBq/kg of patient weight.

**Results:** The patients were in average 48 years old; the youngest 22 and the oldest 80 years old.

Changes compatible with sarcoidosis were detected in all patients on the first PET-CT investigation.

On the suggestion of the attentive PET-CT scan reading malignant disease was in subsequent diagnostic process confirmed in 5/124 patients (in 4,0 %). In 4 patients malignant disease (breast cancer, colorectal carcinoma, spleen lymphoma and appendiceal carcinoid) was discovered due to the initial PET-CT report and in 1 patient malignancy (prostatic cancer) was discovered on the basis of the second PET-CT report.

Changes suspected for malignancy were not discovered on PET-CT investigation in any of 4 patients (in 3,2 %) with known and already treated malignant disease.

### **Conclusion:**

Based on attentive PET-CT scan readings malignant disease was found in its early stage in 4 % of patients with sarcoidosis.

**A CASE OF NEUROBLASTOMA IN A 7 YEAR OLD CHILD**  
**A.TODOROV, L. CHERVENKOV, V.SIRAKOV, M. STOEVA, K. VELKOVA**  
**Medical University - Plovdiv**  
**Medical Imaging Department**

Neuroblastoma is a neuroendocrine tumor - the most common extracranial solid malignant tumor in childhood. Nearly half of the neuroblastomas are in children younger than 2 years. In most of the cases neuroblastomas originate from one of the adrenal glands, but can also be developed by the nerve tissue in the neck, thorax, abdomen and pelvis, all areas of the sympathetic nervous system from neck to pelvis. The most common location of neuroblastoma is the adrenal glands followed by: neck (1%), breast (19%), abdomen (30% without adrenal glands) or pelvis (1%).

Neuroblastoma often causes metastases in other parts of the body prior any symptoms. 50 – 60% of all cases are presented with metastases.

Neuroblastoma etiology is not clearly defined. Most of the cases are sporadic and non-family related. 1-2% of the cases are registered in families and related to certain genome mutations. Family neuroblastoma is caused by rare mutations of the ALK gene.

This paper presents a case of a 7 year old child with a trauma in the left lumbal area, with severe abdominal pain. The child is hospitalized following an abdominal CT and suspicion for intraperitoneal hematoma. Dynamically – 39 degrees fibril, strong headache, vomiting and no appetite. The CT exam verified the retroperitoneally located heterogenous tumor formation located to the left with size 129/93 mm, dislocated left kidney, pancreatic body and tail, passing in front of the abdominal aorta and reaching porta hepatis. Lymph nodules set has been registered. Following an operative intervention, a verification of the diagnosis was reached – neuroblastoma chromatin++ , CD4 – NSE.



# INFLUENCE OF NATURAL RADIOACTIVITY OF LUTETIUM IN THE PET DEVICES WITH LSO SCINTILLATORS

Antic V.<sup>1,2</sup>, Stankovic K.<sup>2</sup>

<sup>1</sup>Center for Nuclear Medicine, University Clinical Centre of Serbia, Belgrade, Serbia,

Pasterova 2, 11000 Belgrade

<sup>2</sup> School of Electrical Engineering, University of Belgrade, Bulevar kralja Aleksandra 73, 11120 Belgrade

**Introduction:** The current PET devices contain scintillation crystals based on lutetium - LSO or LYSO. Lutetium <sup>175</sup>Lu is incorporate with radioactive <sup>176</sup>Lu (abundance 2.6%;  $T_{1/2}=(3.56\pm0.07)\times10^{10}$  years;  $\beta$ - radiation ( $E_{max}=596\text{keV}$ ), followed by three simultaneous  $\gamma$ -ray emissions (energies: 88, 202 and 307keV)). Taking into account long half-life, lutetium activity could be considered as constant -  $52.61\pm0.36\text{Bq/g}$ .

**Objective:** The objective of this paper is to estimate the amount of radioactive lutetium in PET-CT device from Clinical Centre of Serbia (with LSO detectors), and potential impact on the diagnostic information.

**Methods:** Based on the dimensions of the crystal, mass number and the total number of crystals, it was estimated the share of isotope <sup>176</sup>Lu in the overall mass, and the associated radioactivity.

**Results:** According to the device technical specification, it was determined the detector size and calculated the mass of detector unit - 2,368g. Furthermore, there is 169 crystals per detector block and 144 detector blocks, which leads to the total detector mass - 57627g, from which the share of <sup>176</sup>Lu is 1150g. Hence, there is ring distributed radioactivity of about 60.5kBq.

**Conclusion:** Natural radioactivity of lutetium poses no problem in clinical PET imaging (excitation activities  $\sim100\text{MBq}$ , energy threshold 350keV), but could have influence on the QC examinations with low activities, with <sup>68</sup>Ge point source (activity  $\sim5\text{kBq}$ ), and potentially at the end of dynamic studies using <sup>11</sup>C or <sup>15</sup>O. After replacement of the detector block or termination of device exploitation, the proper disposal of detector crystals is necessary.

## QUANTITATIVE ASSESSMENT OF VASCULAR TRANSIT THROUGH KIDNEY: RUTLAND-PATLAK ANALYSIS OF INITIAL PART OF RENOGRAM

Beatović S<sup>1</sup>, Jakšić E<sup>1</sup>, Janković M<sup>2</sup>, Antić V<sup>3</sup>, Šobić-Šaranović D<sup>1</sup>, Artiko V<sup>1</sup>.

1. University of Belgrade, Faculty of Medicine, Center for Nuclear Medicine, Clinical Center of Serbia
2. University of Belgrade, Faculty of Electrical Engineering
3. Center for Nuclear Medicine, Clinical Center of Serbia  
Belgrade

This study **aimed** at evaluating the technique of renal blood flow (RBF) estimation by implementation of Rutland-Patlak (RP) analysis to initial part of renogram.

**Subjects and Method:** 54 subjects were investigated: 20 potential kidney donors (Group A, control group), 20 patients with well-functioning transplant (Group B) and 14 patients with suspected acute rejection (Group C). Dynamic scintigraphy was done 22 minutes after bolus of 370 MBqTc-99m MAG3. Regions of interest (ROI) were outlined over left ventricle, right lung and kidneys, and for transplanted kidney, over kidney graft and abdominal aorta. RBF was estimated from first pass activity plateau in renal ROI, as the difference between maximal slopes of renal and arterial curves, and expressed as percentage cardiac output (CO).

**Results:** In group A, RBF was  $18.28\% \pm 3.65\%$  CO for both kidneys and  $9.14\% \pm 2.15\%$  CO for one kidney. Transplant blood flow (TBF) in group B was  $13.99\% \pm 2.29\%$  CO, and in group C  $6.11\% \pm 2.27\%$  CO. It was 66% lower than in group A and 56% lower than in group B. Statistical difference between A/C and B/C was significant ( $p < 0.005$ ). The highest value in group C of 7.93% CO was lower than the lowest value in group B (9.62% CO).

**Conclusion:** Fractional RBF, derived from upslope ratio of kidney curve and arterial curve is sensitive method for quantifying renal perfusion. In healthy individuals physiological values of RBF were obtained. Well-functioning transplants receive fraction of CO similar to that delivered to two normal kidneys. Flow to rejecting allograft is significantly reduced.

# ADVANCED QUANTITATIVE ANALYSIS OF DYNAMIC RENAL SCINTIGRAPHY: ROLE OF PHYSIOLOGIC PARAMETERS OF KIDNEY OUTPUT IN THE DIAGNOSIS OF UPPER URINARY TRACT OBSTRUCTION

Beatović S<sup>1</sup>, Jakšić E<sup>1</sup>, Janković M<sup>2</sup>, Radulović M<sup>3</sup>, Šobić-Šaranović D<sup>1</sup>, Artiko V<sup>1</sup>

1. University of Belgrade, Faculty of Medicine, Center for Nuclear Medicine, Clinical Center of Serbia
2. University of Belgrade, Faculty of Electrical Engineering
3. Military Medical Academy, Belgrade

**Objectives** of this study were to implement new algorithms for quantitative analysis of dynamic renal scintigraphy, and to analyze significance of output efficiency and normalized residual activity in distinguishing between obstruction and non-obstructive dilatation.

**Subjects and methods:** 183 patients (mean: 51.8 years) underwent <sup>99m</sup>Tc DTPA dynamic scintigraphy with furosemide stimulation (F+20). 323 kidneys were analyzed, and according to assessment of images and renograms, were classified as normal (77), unobstructed (143), obstructed (65) and equivocal (38). International Atomic Energy Agency (IAEA) Software was applied to process studies. Parameters analyzed were: output efficiency at 20 minute (OE<sub>20</sub>), and 20 minutes after furosemide (OE<sub>F+20</sub>), normalized residual activity at 20 minute (NORA<sub>20</sub>) and on post-micturition acquisition (NORA<sub>PM</sub>).

**Results** were presented as follows (mean±SD): normal kidneys: OE<sub>20</sub>: 88±5%, OE<sub>F+20</sub>: 95±4%, NORA<sub>20</sub>: 0.70±0.23, NORA<sub>PM</sub>: 0.07±0.03; unobstructed kidneys: OE<sub>F+20</sub>: 93±2%; NORA<sub>PM</sub>: 0.08±0.02; obstructed kidneys: OE<sub>F+20</sub>: 79±7%; NORA<sub>PM</sub>: 0.22±0.09. Difference obstruction/dilatation was significant (p<0.001). Linear regression between OE<sub>20</sub> and NORA<sub>20</sub> was significant (r= -0.972). ROC analysis revealed cutoff values for obstruction at 88% and 0.145 for OE<sub>F+20</sub> and NORA<sub>PM</sub> respectively. Among 38 kidneys with equivocal findings, 28 kidneys showed both OE<sub>F+20</sub> and NORA<sub>PM</sub> in “non-obstructive” range, in 9 kidneys both parameters showed “obstructive” values, and in one kidney, OE<sub>F+20</sub> indicated obstruction, but, NORA<sub>PM</sub> revealed non-obstructive pattern.

**Conclusion:** Implementation of new algorithms for quantitation of renogram improves diagnostic utility of renography. OE<sub>F+20</sub> and NORA<sub>PM</sub> are sensitive and specific indices of kidney washout. They contribute to diagnosis of kidney obstruction and help to clarify indeterminate diuresis renography findings.

## **Whole body and finger effective dose for medical workers operating in a PET/CT department with statistical analysis**

**Dalianis K<sup>1</sup>, Kollias G<sup>1</sup>, Vlachou F<sup>2</sup>, Filippi V<sup>2</sup>, Andreou J<sup>2</sup>, Efthymiadou R<sup>2</sup>, Prassopoulos V<sup>2</sup>**

**<sup>1</sup>Medical Physics Department ,Hygeia S.A., Athens, Marousi, <sup>2</sup>PET/CT Department, Hygeia S.A., Athens, Marousi**

### *Abstract:*

**Aim:** The PET/CT applications have been continuously increasing for diagnostic procedures. Although such an increase is a positive trend for the benefit of patients, the associated risk of radiation exposure of staff needs to be properly evaluated. The aim of this study was to measure the radiation exposure of the staff and evaluate the doses. **Material-Method:** To estimate the effective dose from external exposure all 6 members of the staff had TLD badges worn at the upper pocket of their overall, TLD rings on the second finger of each hand consisting of disk measuring diameter by 0,9 mm thickness. The basic stages for the PET/CT procedures involve 4 steps: segmentation of the dose, injection of the radiopharmaceutical, nursing care during uptake and positioning of the patient. **Results:** The results of our study for the average cumulative whole body dose for 100 patients ( $\mu\text{Sv} \pm \text{SD}$ ) at different stages were: segmentation of the dose  $189 \pm 7,23$ , injection of the radiopharmaceutical  $245 \pm 6,67$ , nursing care during uptake  $70 \pm 5,63$ , positioning of the patient  $146 \pm 12,3$ . The statistical analysis showed small differences between stages 1, 2 and 4 ( $p > 0,05$ ) but a great statistical difference was observed between stages 2,3  $p = 0,023$ . The results for the finger doses ( $\mu\text{Sv} \pm \text{SD}$ ) regarding the same stages were: segmentation of the dose  $284 \pm 77,4$ , injection of the radiopharmaceutical  $225 \pm 62,3$ , positioning of the patient  $26,79 \pm 5,87$ . **Conclusion:** The personnel dose results are significantly lower than the recommended annual dose by International Commission for Radiological Protection. However a greater effort should be made to reduce the doses further in line with the ALARA principle.

## OCCUPATIONAL EXPOSURE IN PET/CT DIAGNOSTICS: WHOLE BODY AND EXTREMITY DOSES

Antic V.<sup>1,2</sup>, Ciraj-Bjelac O.<sup>2,3</sup>, Stankovic J.<sup>2,3</sup>, Arandjic D.<sup>2,3</sup>, Bozovic P.<sup>2,3</sup>

<sup>1</sup>Center for Nuclear Medicine, University Clinical Centre of Serbia, Belgrade, Serbia,

Pasterova 2, 11000 Belgrade

<sup>2</sup> School of Electrical Engineering, University of Belgrade, Bulevar kralja Aleksandra 73,

11120 Belgrade

<sup>3</sup>Vinča Institute of Nuclear Sciences, University of Belgrade, Mike Petrovica Alasa 12-14,

11001 Belgrade

**Introduction:** The most widely used radiopharmaceutical for clinical PET/CT applications is FDG (2-deoxy-2-(<sup>18</sup>F) fluoro-D-glucose), producing high energy annihilation photons of 511 keV, which yields to a relatively high radiation exposure to nuclear medicine staff, due to manipulation of unsealed radiation sources (container opening, separation and application) and interactions with radioactive patients - especially during patient positioning for imaging.

**Objective:** The objective of this work is to evaluate and analyze radiation exposure levels for medical staff working in National PET centre in Serbia in terms of whole body and extremity dose.

**Methods:** Dosimeters TLD-100 (LiF: Mg, Ti) were used for whole body dose measurements, while DXT-100 (LiF: Mg, Ti) dosimeter were used for extremity dosimetry. Dose values, both in terms of Hp(10) and Hp(0.07) were measured during 7-month period and results were normalized to the total manipulated activity (μSv/GBq).

**Results:** Dose per unit activity for Hp(10) is estimated to be 57 μSv/GBq. The average dose per procedure in terms of Hp(10) was 21 μSv, whereas the extremity dose in terms of Hp(0.07) was 159 μSv/procedure (assuming injected activity of 370 MBq). Extrapolated annual whole body dose (2000 procedures) is estimated to 3.4 mSv, while corresponding extremity dose would be 26 mSv.

**Conclusion:** Although the individual doses are within the regulatory limits, the increase in workload would result in higher staff doses. An effort must be made to review the working procedure and reduce the radiation dose as low as reasonably achievable.

## **THE BENEFITS OF ISO/IEC 17025 ACCREDITATION OF RADIOPHARMACY LABORATORY**

**Apostolova Paulina, Sterjova Marija, Smilkov Katarina, Gorgieva Ackova Darinka, Delipetrevva Katarina, Janevik Ivanovska Emilija  
Faculty of Medical Sciences, University Goce Delčev – Štip**

Laboratory is a part of the Department of Pharmacy in the Faculty of Medical Sciences, at the Goce Delcev University in Štip. Main activities are focused on improving knowledge for radiopharmacy of bachelor students, master students and doing PhD thesis. Also, we are trying to provide services for external associates as a testing laboratory.

As a developing country, we are facing with the begging's of the process of accreditation. The accreditation process is a lengthy and time consuming method. There isn't specific time frame for preparation for accreditation.

We incorporate an overall system for technical and quality management, which results in benefits observed in daily laboratory practices. With ISO 17025 standard incorporation we achieve traceability of the whole documentation, daily good working plan, including preventive and corrective actions and we are doing training and education of laboratory stuff for better work conditions and best protection.

Benefits of getting MKC EN ISO/IEC 17025 certificate can be differentiate on three different angles: benefits of customers, laboratory personnel and laboratory itself. Our first aim is to show to the customers the benefits obtained from uniformity, quality, precision and confidence of developed results in our laboratory. Other benefits for laboratory are International Recognition, Prevents Defects, Increased Accuracy, Cost Savings and Reduced Waste.

Laboratory accreditation is a challenging process and the commitment of top management and staff involvement will determine the success of its implementation. Future perspectives are to became part of proficiency testing and begin to use validate methods.

## **ESTABLISHMENT OF PRODUCTION LABORATORY FOR FLUORODEOXYGLUCOSE 18F (18F-FDG)**

**Marija Atanasova, Maja Jancovska, Katerina Kolevska, Maja Velickovska, Filip Jolevski, Emilija Janevik-Ivanovska**

**Faculty of Medical Sciences, Unit for PET implementation, University Goce Delčev – Štip**

The radiopharmaceuticals such as  $^{18}\text{F}$ -FDG are sterile radioactive products for human use and because of that production procedure is subject to special requirements. To minimize risks of radiation the production is fully automated in specially designed laboratories. On the other hand to minimize the microbiological and pyrogenic contamination during the production, all production steps should be carried out in clean areas entry to which should be through airlocks for personnel, equipment and materials. The production of  $^{18}\text{F}$ -FDG should be carried out under negative pressure surrounded by a positive pressure zone ensuring that appropriate air quality requirements are met according EN ISO 14644-1

Due to this requirements our laboratory is specially designed to ensure fully automated and safe production of  $^{18}\text{F}$ -FDG, taking care of radiation protection and sterility. For this purpose is equipped with double horizontal BBS1-SY hot cell shielded box designed to house automatic modules intended for routine production with two Synthera modules for  $^{18}\text{F}$ -FDG synthesis, which are multi-purpose fully automated synthesizers. For dispensing of FDG we have hot cell for aseptic radiopharmaceutical dispensing Talia with Class A laminar flow equipped with CLIO - automatic dispensing system for radiopharmaceuticals, designed for dispense vials and syringes.

To ensure the safe manufacture of  $^{18}\text{F}$ -FDG radiopharmaceuticals, validation and qualification will be applied in accordance with the principles of good manufacturing practices (GMP). All personnel for production will be trained in GMP, the safe handling of radioactive materials and radiation safety procedures.

## **QUALITY CONTROL OF PET RADIOPHARMACEUTICALS, AN IMPERATIVE FOR SUCCESSFUL CLINICAL OUTCOMES**

**Maja Velickovska, Filip Jolevski, Marija Atanasova, Maja Jancovska, Katerina Kolevska, , Emilija Janevik-Ivanovska**

**Faculty of Medical Sciences, Unit for PET implementation, University Goce Delčev**

Radiopharmaceuticals are undergo strict quality control (QC) tests and procedures as well as nonradioactive sterile pharmaceuticals since they are intended for intravenous administration to humans. In addition, tests for radionuclidic and radiochemical purity have to be carried out. Basically, quality control involves several specific tests and measurements that ensure the purity, potency, product identity, biologic safety, and efficacy of PET radiopharmaceuticals. QC of PET radiopharmaceuticals should be performed in accordance with specific monographs of official pharmacopoeias and national pharmaceuticals/radiopharmaceuticals regulation. In absence of specific pharmacopoeia monographs, the testing protocol should take in consideration the requirements of radiopharmaceutical's general monograph. If the methods are non-pharmacopoeia, they should be validated.

The quality control tests fall into two categories: physicochemical tests and biological tests. The physicochemical tests indicate the level of radionuclide, radiochemical and chemical impurities, and determine the pH, ionic strength, osmolality. The biological tests establish the sterility and apyrogenicity. Unlike other pharmaceuticals, QC of PET radiopharmaceuticals is done in a specific way because of the radioactivity and the short half-life of used PET radionuclides versus duration of the execution of some of the tests. The individual monographs indicates the tests that need not to be completed before release for use. These tests then constitute the QC of the product.

QC of PET radiopharmaceuticals is essential part of radiopharmaceutical's production in terms of assuring safety of the patient, quality and efficacy of the product and successively, positive impact on the imaging quality.



## **THE NEED OF RADIOPHARMACY IN NUCLEAR MEDICINE DEPARTMENTS: AFRICAN EXPERIENCE**

**Joel Munene Muchira<sup>1,3</sup>, David Mwanza Wanjeh<sup>1,3</sup>, Aschalew Alemu<sup>2,3</sup>, Emilija Janevik-Ivanovska**

<sup>1</sup>**Ministry of Health, Kenya**

<sup>2</sup>**Faculty of Medicine, Addis Ababa**

<sup>3</sup>**Faculty of Medical Sciences, Goce Delcev University, Shtip**

The current status of Radiopharmacy Practice of Kenya and Ethiopia is our starting point for creating our vision of perspective of well recognized qualified professionals in the field.

The exact information on the number, status and size of Radiopharmacy units, regionally, is still not clearly documented, as well human resources, education, suitable training and local demand for the Radiopharmacy and Nuclear Medicine services. It is the existence of this gap that necessitated the preparation of this presentation.

The Radiopharmacy Practice requires well-defined and controlled conditions to avoid the risk contamination with microbes, pyrogens and particulate matter as well as cross contamination with other radiopharmaceuticals.

Corresponding to the expected improvement, the principles of Good Practices in all levels should be planned, introduced by the planned priority and strictly observed in the production, preparation, testing and the packaging of the final product ready for use.

Almost all used radiopharmaceuticals are parenterally administered and for that reason must to be prepared using techniques and procedures, that guarantee sterility of the product. Every procedure undertaken should be done according to the clearly defined protocol and under the right conditions so as to build quality into the product.

Radiopharmacy professionals should have adequate training in all aspects of sterile production, quality control, GMP, GLP, radiation safety and radiochemistry to ensure that they are competent to handle radioactive materials and that they can take responsibility for their level of practice.

We are expecting that our education and experience during our Master program in the Goce Delcev University will support our idea how to create the network of all professionals and state authorities for establishing and develop Good Radiopharmacy Practice, qualified personnel and appropriate regulation according to the local and international parameters will be step forward to have advanced health care system and confidence of the patients.

## **Comparison between 18F-FDG-PET/CT and somatostatin receptor scintigraphy in a patient with a neuroendocrine tumor**

**Petrov T<sup>1</sup>, Garcheva M<sup>1</sup>, Elenkova A<sup>2</sup>, Vasilev V<sup>2</sup>, Ivanova R<sup>2</sup>, Zacharieva S<sup>2</sup>, Kostadinova I<sup>1</sup>**

**<sup>1</sup>Clinic of nuclear medicine, Medical University, Sofia; <sup>2</sup>Clinical center of endocrinology, Medical University, Sofia**

A forty-year-old patient presented with cough, dyspnea, orthostatic hypotension, significant weight loss and bilateral axillary lymphadenomegaly. Lymph node biopsy was performed which revealed low differentiated neuroendocrine carcinoma (NEC) with high proliferation activity (Ki67>25%) and synaptophysin expression in 100% of the tumor cells. A contrast computed tomography was performed for the primary tumor detection, which visualized a left adrenal tumor mass. Urinary methanephrine and catecholamine were within normal ranges. Serum chromogranin A and 5-hydroxy-indoleacetic acid levels were elevated. Further examinations executed for staging of the disease were Somatostatin receptor scintigraphy (SRS) with 99m Tc-tectrotide - SPECT/CT and 18F-FDG-PET/CT.

Results and conclusion: The SRS detected lesions with expression of the somatostatin receptors in the left lung, in right axillary lymph nodes, in the anterior chest wall (subcutaneous) and in supraclavicular lymph node. FDG-PET/CT proved high metabolic activity in the left lung, left adrenal gland, in additional mass between the left kidney and the spleen, axillary lymph nodes, more subcutaneous nodes, peritoneal lesion and solitary bone marrow lesion. The combination of SRS and FDG-PET/CT confirmed the diagnosis neuroendocrine carcinoma and helped the staging of the disease as well as the decision about the patient therapy, specifying differentiated and dedifferentiated tumor lesions.

## Correlation of Brain perfusion SPECT using $^{99m}\text{Tc}$ -HMPAO with neuropsychological tests in diagnosis of Dementia

Makazlieva T.<sup>1</sup>, Vaskova O.<sup>1</sup>, Krsteska R.<sup>2</sup>, Stoeva M.<sup>2</sup>, Zafirova-Ivanovska B.<sup>3</sup>, Mukaetova Ladinska E.<sup>4</sup>

<sup>1</sup>Institute of Pathophysiology and Nuclear Medicine, Medical Faculty, Skopje

<sup>2</sup>Psychiatric Hospital, Psychogeriatric Center – Skopje

<sup>3</sup>Institute of Epidemiology and Biostatistics, Medical Faculty, Skopje

<sup>4</sup>Institute for Ageing and Health, Newcastle University

### Abstract

**Introduction:** Dementia is clinical syndrome, manifested as multiple cognitive failure. Due to still insufficiently elucidated pathophysiology and the need to develop an effective therapy, there is interest in early diagnosis of pre-demented state.

**Aim:** We have set the objective to evaluate the correlation of findings from neuropsychological tests Mini Mental Test (MMCE), Boston Test (BNT) and Clock drawing test (CDT) with findings from brain  $^{99m}\text{Tc}$ -HMPAO SPECT studies.

**Materials and methods:** The study included 11 patients, selected by specialist psychiatrist, after clinical examination. In all patients was preformed  $^{99m}\text{Tc}$ -HMPAO SPECT brain scintigraphy. Results of the brain perfusion were classified according to extent of perfusion defects. MMSE, BNT and CDT scores were also graded. Statistical analysis is conducted by determining the Spearman Rank correlation coefficient between the parameters.

**Results:** Correlation between MMSE and BNT scores and extent of SPECT perfusion defects is positive and statistically highly significant, while CDT shows positive, but statistically insignificant correlation.

**Conclusion:** Findings of all the evaluated patients showed indisputable defects in perfusion which in correlation with clinical criteria give useful guidance in diagnosis of dementia. The sample was statistically small, it is necessary to include a larger group of patients for more relevant conclusions.

## **POSITRON EMISSION TOMOGRAPHY WITH 18F- FLUORODEOXYGLUCOSE IN THE DIFFERENTIAL DIAGNOSIS OF PARKINSONISM**

**L. Brajković<sup>1</sup>, V. Kostić<sup>2</sup>, M. Svetel<sup>2</sup>, E. Stefanova<sup>2</sup>, I. Petrović<sup>2</sup>, M. Jecmenica-Lukić<sup>2</sup>,**

**D. Šobić-Šaranović<sup>1</sup>, V. Artiko<sup>1</sup>**

**Center for Nuclear Medicine<sup>1</sup>, Clinical Center of Serbia,  
Clinic for Neurology<sup>2</sup>, Clinical Center of Serbia, Belgrade  
lelabrajko62@gmail.com**

**Introduction:** Positron emission tomography (PET) using 18F-fluorodeoxyglucose (FDG) shows a characteristic pattern of regional glucose metabolism in idiopathic Parkinson's disease (IPD) and atypical Parkinsonian syndroms: multiple system atrophy (MSA), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD) as the most common form of neurodegenerative parkinsonism.

**Objective:** To show the characteristic patterns of regional glucose metabolism in different forms of parkinsonism and assess their utility in the differential diagnosis of individual patients with clinical parkinsonism. **Patients and methods:** FDG-PET scan was performed on 72 patients (age 40-81) referred by specialists in movement disorders with clinical diagnosis of IPD(29), MSA(20), PSP(21), CBD(2). FDG-PET findings were interpreted visually and using the SPM analysis. Imaging based diagnosis and clinical diagnosis were compared.

**Results:** IPD characterized by preserved and pronounced glucose metabolism in the basal ganglia with preserved cortical metabolism or reduced metabolism frontal (medial and lateral premotor) or parietal and posterior parietotemporal if the patient has cognitive disorders. MSA- hypometabolism in the striatum especially putamen, cerebellar and brainstem level (pons), and usually frontal cortical (basal, dorsolateral) and insular. PSP -hypometabolism glucose frontal (medial, basal, lateral premotor), insular, thalamic and striatal-caudate, CBD- asymmetrical glucose hypometabolism cortical and subcortical are most notable frontoparietal in the hemisphere contralateral by the dominant clinical symptomatology. Concordance of imaging and clinical diagnosis was obtained in IPD(93 %), MSA(90 %), PSP(95%), CBD(100%).

**Conclusion:** Our results suggest that FDG-PET characteristic metabolic pattern of the regional glucose metabolism may help in the differential diagnosis of some Parkinsonian syndroms in clinical practice.

## **ROLE OF FCH-PET/CT IN BRAIN LESIONS ASSESSMENT**

**Nikaki A<sup>1</sup>, Savvidou D<sup>1</sup>, Prassopoulos V<sup>1</sup>, Filippi V<sup>1</sup>, Tsougos I<sup>2</sup>, Vlachou F<sup>1</sup>, Andreou I<sup>1</sup>, Pipikos T<sup>1</sup>, Dalianis K<sup>3</sup>, Papoutsis V<sup>1</sup>, Efthymiadou R<sup>1</sup>, Georgoulas P<sup>4</sup>;**

**<sup>1</sup>PET/CT Department ,Hygeia S.A., Athens, Marousi, <sup>2</sup>Medical Physics Department ,University of Thessaly, Larissa, <sup>3</sup>Medical Physics Department ,Hygeia S.A., Athens, Marousi, <sup>4</sup>Nuclear Medicine Department, University of Thessaly, Larissa**

**Objectives:** to evaluate FCH-PET/CT in the assessment of brain lesions.

**Methods:** 11 patients (4 recurrent primary brain tumor grade III-IV, 3 metastatic, 2 neurological symptoms/MRI findings, 2 cerebral NHL) underwent FCH-PET examinations for evaluation of 19 findings in MRI. 4 patients had never received any prior treatment for brain lesions, 7 had received therapy according to their disease. Findings in FCH-PET fused with MRI were evaluated visual and semiquantitatively using SUVmax and tumor-to-background ratio (T/B: SUVmax of tumor/SUVmean of background).

**Results:** FCH-PET was true positive in 2 cases of recurrent disease (3 lesions, average SUVmax  $2.6 \pm 0.75$ , average T/B  $8.8 \pm 3.4$ ), in 2 cases of metastatic tumors (5 lesions, average SUVmax  $3.3 \pm 3$ , average T/B  $7.9 \pm 6$ ), in 1 case of neurologic symptoms, in 1 NHL. All patients with true-positive findings received therapy after FCH-PET. FCH-PET was true negative in 2 cases of primary brain tumors and in 1 NHL (patients were put under surveillance). In one case of metastatic brain tumor, MRI showed angioedema while PET diffuse slightly increased uptake of FCH (the patient had also torso findings and received treatment). FCH-PET was false negative in one case of neurologic symptoms as MRI was indicative of gliomatosis. Using paired t-test statistically significant differences were recorded between SUVmax and T/B values for metastatic lesions ( $p < 0.05$ ). Average SUVmax between primary and metastatic lesions did not significantly differ.

**Conclusion:** With respect to our small inhomogeneous sample and the referral bias, our results indicate that <sup>18</sup>F-FCH- PET, may serve as complementary tool in brain tumor imaging.

## **PET AND MRI IN THE DIAGNOSTIC ALGORITHM OF PATIENTS WITH DRUG-RESISTENT EPILEPSY**

Kostadinova I<sup>1</sup>, Minkin K<sup>2</sup>, Dimova P<sup>2</sup>, Zlatareva D<sup>3</sup>, Hadjiiska V.<sup>1</sup>

<sup>1</sup> Department of Nuclear Medicine, <sup>2</sup> Department of Neurosurgery, <sup>3</sup> Department of Radiology, Medical University, Sofia

### **Aim**

The aim of our study was to try to find the place of PET and MRI, compared to invasive EEG, as a reference tool, in the diagnostic algorithm of patients with drug-resistant epilepsy.

### **Material and methods**

Twenty two patients with drug-resistant epilepsy were evaluated with MRI, 18F-FDG PET/CT / 18F-FDG activity 150-200 MBq / and invasive EEG. PET/CT study was fused with 3D MRI, using FSL or GE software.

### **Results**

Both MRI and PET were normal in 4 patients. From the remaining 18 patients there were 5 patients with normal MRI and abnormal PET-CT demonstrating hypometabolism. There was partial or complete congruence between the zones of PET hypometabolism and the seizure onset zone defined by invasive EEG in 17/18 patients. There was only 1 patient with discrepancy between the zone of hypometabolism on PET/CT and the seizure onset zone defined by invasive EEG. MRI was normal in 9 patients and structural lesions were identified in 13 patients. Partial or complete overlapping between the lesion and the seizure onset zone was observed in 11/13 cases with MRI lesion. In other 2 cases there was no overlapping between the data from invasive EEG and the MRI lesion. Fourteen patients were operated on and satisfactory seizure control was achieved in 10 patients.

### **Conclusion**

We consider, that 18F-FDG PET/CT is a sensitive non invasive tool for defining the epileptogenic zone in patients with drug-resistant epilepsy and according to our first experience it is more accurate than MRI. It has to be applied in all cases with normal findings on MRI.

# QUANTITATIVE MEASUREMENTS OF THE THERAPEUTIC EFFECT IN PATIENTS WITH SOMATOSTATIN EXPRESSING TUMORS, USING 99mTc-TECTROTYDE

Kostadinova I., A.Demirev, Medical Faculty, Sofia

## Aim

The aim of our study was to introduce quantitative measurements in addition to the usual qualitative criteria for a precise evaluation of the response to the applied therapy in patients with somatostatin receptor expressing (SR) neuroendocrine tumors.

## Material and method

We have performed in total 54 examinations on 22 patients (15 of them were examined twice, 7 of them triple ) after 3-12 cycles of sandostatine therapy, using the somatostatin analog 99mTc-HYNIC-TOC (Tektrotyd,PL) in activity between 370-550 MBq. Whole body/spot and hybrid imaging investigation - SPECT-CT were performed 2- 4h p.i. For a quantitative measurement of the degree of activity of the radiopharmaceutical in them / compared to background /, an index of activity /IA/ was introduced, calculated in 1-5 target lesions.

## Results

In 19/22 of the investigated patients, it was difficult to evaluate therapeutic response, relying only on qualitative criteria, especially in those with multiple pathological lesions. In 9 of all patients, there was a partial therapeutic response with an average decrease of IA with 35.6% (calculated as a sum of IA of the all affected structures) ; in 3-complete response (without any pathological uptake); in 6 -stable disease with IA change between -12% and + 11%; in 4 of the patients –progressive disease with IA increase with 34.5%.

## Conclusion

We suggest that applying additional quantitative criteria to the routine qualitative one in patients SR – tumors, using 99mTc-HYNIC-TOC, helps for a more precise evaluation of the therapeutic effect, especially in those with an advanced disease.

## THE ROLE OF FDG PET/CT FOR RE-STAGING IN BREAST CANCER PATIENTS WITH ELEVATED SERUM TUMOR MARKER LEVELS

Yüksel M<sup>1</sup>, Yanmaz MT<sup>2</sup>

Kemerburgaz University, School of Medicine, Nuclear Medicine<sup>1</sup>, Medical Oncology<sup>2</sup>, Istanbul

**Aim:** Confirmation of suspicious relapse and/or metastasis in breast cancer patients (BC-pts), with elevated tumor markers is important for patient management. In this study, we aimed to evaluate the role of FDG PET/CT in re-staging of BC-pts with elevated serum tumor markers (with or without radiological or bone scan findings) in the follow-up period. **Materials and Method:** A total of 45 BC-pts with elevated serum tumor marker levels in the follow-up period were evaluated with FDG PET/CT for re-staging. Medical records of all patients were evaluated retrospectively. **Results:** FDG PET/CT was positive in 37/45 (82%) and negative in 8/43 (18%) BC-pts. Distribution of metastasis was as follows; 23/45 bone, 8/45 liver, 10/45 lung, 19/45 lymph nodes, and 2/45 pleura. **Conclusion:** According to our findings, FDG PET/CT seems to have important contribution in the evaluation of BC-pts with elevated serum tumor marker levels. As it allows whole-body scanning in a single session, FDG PET/CT could be a time-saving imaging modality in BC-pts with elevated serum tumor marker levels. However, our suggestion needs to be confirmed with further investigations in larger number of BC-pts with elevated serum tumor marker levels.



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## **F-18 FDG PET/CT in evaluation of subcutaneous and muscle metastases from malignant melanoma: case report**

**Muratovska L, Crcareva B, Stojanovska L, Anastasov Gj, Bogojevska J**

**Clinical Hospital Acibadem Sistina, Skopje**

**Introduction:** Malignant melanoma, although only 4% of all skin cancers, has a high rate of mortality (80%), but if detected at an early stage can be cured. It is characterized by variations in their biological behavior and therefore can be spread to every organ. The most common sites of metastasis are the skin, subcutaneous tissue, lymph nodes, then the lungs, liver, brain, bone and intestine. Subcutaneous and skeletal muscles metastases of melanoma in clinical practice are rare and only sporadically reported in the literature. Usually occur later and are a sign of disease progression. Usually subcutaneous and muscle metastases are painful and if multiple are difficult to diagnose. They use different methods of diagnosis, but none lacks accuracy for their confirmation and confirmation of their dissemination. By applying the fluorine-18 fluoro-2-deoxy-D-glucose- positron emission tomography/ computed tomography (FDG-PET / CT) which is an important application in oncology, increases diagnostic accuracy of subcutaneous and muscle melanoma metastasis. FDG-PET / CT show changes in the whole body with one scanning. Still the gold standard for confirmation of the diagnosis is a biopsy.

**Objectives:** To present the case of a patient with malignant melanoma and multiple subcutaneous and muscle metastases detected by FDG-PET / CT.

**Case:** 61 year old patient referred for FDG-PET / CT scan at our hospital by his oncologist. In 2009 - surgery of malignant melanoma of the neck skin. According to the patient's, postoperative findings are normal. Regular studies has been performed with CT scan of chest and abdomen and MRI of the brain. In December 2014 the occurrence of bloody stools, therefore he was studied by a gastroenterologist and seen a change in the small intestine which is operated and confirmed metastatic deposit of malignant melanoma. In March 2015 performed FDG PET / CT scan at our institution. The scan did not show pathological accumulations of FDG locally on the neck or in the small intestine, but showing metabolic activity in the right adrenal gland, and multiple muscular and subcutaneous accumulations. Subcutaneous nodular lesion in the region of epigastrium was surgical removed. Pathohystology findings confirmed metastasis of malignant melanoma. The patient is ongoing chemotherapy.

**Discussion:** The obtained findings of FDG-PET / CT scan shows that it is superior imaging techniques for early detection of multiple subcutaneous and muscle metastases from malignant melanoma. With one whole body scanning it

differentiate anatomical and functional changes which is very important in the differential diagnosis of subcutaneous / muscle metastases from other soft tissue tumors.

## Value of neutrophil lymphocyte ratio in patients with bone metastases of solid tumors

Caliskan B, Korkmaz AN

Abant İzzet Baysal University, Department of Nuclear Medicine, Bolu

**Introduction and objectives:** It is known that tumors can cause an inflammatory reaction which plays an important role on neoplastic growth. Recently some hematological indices, such as neutrophil counts and neutrophil-to-lymphocyte ratios (NLR), have been introduced as prognostic indicators in cancer patients. In this study, we aimed to investigate any relationship between bone metastases and NLR.

**Methods:** Patients with histologically verified primary solid malignancies, who were referred for bone scintigraphy between January 2012 and December 2013 were reviewed retrospectively. Patients' hematological parameters were obtained from hospital database. Patients were categorized into three groups based on metastatic bone disease with or without other organ metastases. Patients with chronic inflammatory disease, hematological disease and those that were using anti-inflammatory medications were excluded from the study.

**Results:** Scintigraphy results were normal in 147 patients; were suggestive of degenerative changes corroborated with PET/CT and other radiological findings in 24 patients. There were 171 patients with a non-metastatic scan (group A), 25 patients with metastatic bone disease without any other organ metastases (group B) and 48 patients with metastatic bone disease with other organ metastases (group C). The median NLR of the patients were 2.55 (range: 0.38–20.7) in group A, 2.83 (range: 1.56–31.8) in group B and 4.12 (range: 1.79–38) in group C. NLR was significantly higher in group C compared to groups A and B ( $p < 0.001$ ).

**Conclusion:** NLR seems to have a significant association with other organ metastases but not with bone metastases.

## **Evaluation of SPECT/low dose CT Imaging in the assesment of equivocal spine lesions in planar bone scintigraphy**

**Pipikos T<sup>1</sup>, Vlachou F<sup>1</sup>, Nikaki A<sup>1</sup>, Dalianis K<sup>2</sup>, Iakovidou A<sup>1</sup>, Efthymiadou R<sup>3</sup>, V. Prassopoulos V<sup>1</sup>;**

**<sup>1</sup>Nuclear Medicine Department Hygeia SA, Athens, Marousi, <sup>2</sup>Medical Physics Department ,Hygeia S.A., Athens, Marousi <sup>3</sup>CT- MRI Department Hygeia SA, Athens, Marousi**

**AIM:** Bone scintigraphy is used for whole body skeletal staging in cancer patients. One of the method's main disadvantages is low specificity, especially in the spine. With the usage of hybrid SPECT/low dose CT devices, there is the possibility of anatomic localization and further characterization of abnormal tracer uptake foci. In this study we evaluated the effect of SPECT/low dose CT imaging in the assessment of spine scintigraphy abnormalities. **MATERIAL AND METHODS:** We reviewed the planar and SPECT/low dose CT images of 91 patients who underwent bone scan over the last year for malignancy staging and had equivocal spine findings. We examined if SPECT/CT lead to confident diagnosis. Planar and SPECT/CT images were reviewed blinded to each other, by the same nuclear medicine physician. Imaging was performed with a Philips Brightview XCT system.

**RESULTS:** With the application of SPECT/CT, confident diagnosis was established in 71/91(78%) initially equivocal cases. In 62 cases a benign cause of abnormal tracer accumulation was established. In 9 cases diagnosis was changed to bone malignancy. In 20 patients SPECT/CT results did not change equivocal status.

**CONCLUSION:** Bone imaging with SPECT/low dose CT system increases diagnostic confidence and reduces the number of equivocal spine lesions. Equivocal status was preserved in only the 22% of the scans. The majority of the lesions that caused diagnostic problem were proven to be of degenerative origin.

## **SPECT/Low Dose CT Perfusion Study in the Investigation of Suspected Pulmonary Embolism**

**Pipikos T, Vlachou F, Nikaki A, Iakovidou A, Dalianis K, Prassopoulos V;  
Nuclear Medicine Department Hygeia SA, Athens, Marousi**

**AIM:** Ventilation/Perfusion lung scintigraphy is valuable in the assessment of pulmonary embolism. In some cases ventilation study cannot be performed. Modern  $\gamma$ -cameras give the possibility of performing SPECT/low dose CT studies. In this study, we evaluate the performance of this method in the assessment of PE.

**Material and methods:** We studied 72 patients who underwent V/Q lung planar and SPECT study and perfusion SPECT/low dose CT study. Criteria for a positive V/P planar and SPECT study were mismatch of at least one segment or two sub segments that correspond to pulmonary vascular anatomy, while the study was interpreted as non PE when the perfusion was normal and when there was a match or reverse mismatch. The perfusion SPECT/CT study was diagnosed as PE when a segmental or at least two sub segmental perfusion defects with no parenchymal lesions on the low dose CT were found.

**RESULTS:** 21 patients were diagnosed with PE with V/P planar and SPECT method, 1 study was equivocal, while 50 patients were diagnosed as not having PE. With the perfusion SPECT/CT study 23 patients were diagnosed with PE, 48 were normal while 1 was equivocal. There were two false positive findings, one in a patient with central located lung cancer. **CONCLUSION:** Perfusion SPECT/low dose CT study seems to perform quite well in the diagnosis of PE. Although it can't be as accurate as V/P SPECT, it can be of great value in cases that the ventilation study cannot be performed or is unavailable.

## **THE ROLE OF 99mTc-PERTECHNETATE SCAN IN DIAGNOSIS OF MECKEL'S DIVERTICULUM IN ADULT PATIENT: A CASE REPORT**

**Miladinova D<sup>1</sup>. MD PhD, Jankulovski N<sup>2</sup>. MD PhD, Isahi U<sup>3</sup>. MD, Jovanovic R<sup>4</sup>. MD PhD, Trajkovska M<sup>3</sup>. MD PhD, Antovic S<sup>2</sup>. MD**

**<sup>1</sup>Institute of Pathophysiology and Nuclear Medicine, <sup>2</sup>University Clinic for Digestive Surgery, <sup>3</sup>University Clinic for Gastroenterohepatology, <sup>4</sup>Institute of Pathology, Faculty of Medicine, University SsCyril and Methodius, Skopje**

The most common malformation of gastrointestinal tract is Meckel's diverticulum (MD), occurring in 2% of the population. Heterotopic rests of gastric mucosa are seen in 60% of cases with MD. Gastric mucosal secretion can cause peptic ulceration of the diverticulum or adjacent ileum, producing pain, perforation or most commonly bleeding. 60% of patients with complications of MD are under the age of 2 years. Bleeding in MD in adults after age of 40 is unusual.

We present a 33 year old female referred at the Clinic for gastroenterohepatology because of abdominal pain, constipation, fatigue and blood in the stool. Gastroscopy was done previously at the City hospital and was consistent with chronic gastritis. Abdominal ultrasound, colonoscopy and ileoscopy were normal except the small area of prominent vascularization in the distal transversal colon. Capsular endoscopy shown alteration in small bowel mucosa with dominant diverticulum in distal ileal region suggestive for MD. Post contrast NMR of the abdominal region did not show any pathology in the investigated region, including small bowel. Then the patient was referred to the Institute of pathophysiology and nuclear medicine for a 99mTc pertechnetate scan. In fasting condition after intravenous application of 400MBq 99mTc-pertechnetate flow image and subsequent static images were obtained every two minutes during the first ten minutes and every five minutes in the next 20 minutes in anterior position. Additional right lateral, posterior, and oblique images were obtained 15 minutes after the radiopharmaceutical application. Intensive focal accumulation in the right iliac region was evident from the fourth minute (almost at the same time with the appearance of normal gastric mucosa), increasing with the intensity in the subsequent images. The scan finding was consistent with heterotopic gastric mucosa in MD. With two affirmative findings the patient was referred to the digestive surgeon. At the University clinic for digestive surgery, laparoscopic resection with diverticulectomy was done and pathology confirmed the diagnosis of MD with heterotopic gastric mucosa inside.

The 99mTc pertechnetate scan should be considered as a standard method and diagnostic test of choice for preoperative diagnosis of MD.

## **SENTINEL LYMPH NODE IN COLORECTAL CANCER**

**Antovic S<sup>1</sup>, Jankulovski N<sup>1</sup>, Miladinova D<sup>2</sup>, Spasevska L<sup>3</sup>, Stojanovski S<sup>2</sup>, Andreevski V<sup>4</sup>**

**<sup>1</sup>University Clinic for Digestive Surgery, <sup>2</sup>Institute of Pathophysiology and Nuclear Medicine, <sup>3</sup>Institute of Pathology, Faculty of Medicine, <sup>4</sup>University Clinic for Gastroenterohepatology Faculty of medicine University SsCyril and Methodius, Skopje**

The presence of metastasis in the regional lymph nodes is the most important prognostic factor in patients with colorectal cancer. The identification of the sentinel lymph node could significantly improve the accuracy of the analysis and the definite diagnosis in this patients and would undoubtedly influence the decision on appropriate therapy. The Tc99m colloid has been injected around the tumor submucosally, through endoscopy in the amount of 4 ml or one dose of 148 MBq. After the application a selective abdominal imaging on has been done to detect the distribution of the colloid through the lymph nodes to the sentinel node. The patients have been operated on the next day using a standard surgical technique involving complete regional lymphadenectomy. Using a scintillation probe the most radioactive sentinel lymph node was detected and isolated ex vivo, and directed for histopathological analysis.

This prospective controlled study involved 94 patients and 34 of them who have met all inclusion and exclusion criteria have been subjected to a complete clinical protocol. In all patients at least one sentinel lymph node was identified (median number 1.17) which makes for a 100% detection rate. In 31 out of 34 patients the sentinel lymph node has accurately predicted the status of the rest of the regional nodes which makes the accuracy of the method to be at 91.1%. With 3 patients there was a false negative result (the sentinel node was negative while some of the other regional nodes were positive) which makes the sensitivity of the method to be 80% while the negative predictive value is 86.36%. Using immunohistochemistry helped detect micrometastases in 2 patients which would have remained undetected if standard hemotoxillin/eosin staining has been applied. Since 15 patients in this study have been N(+) while 19 N(-) using conventional staining, this has contributed to the upstaging of 10.5% of the patients. In 3 patients the sentinel node, from all the isolated nodes, was the exclusive location where metastases were detected. Aberrant lymphatic drainage was not detected in any of the patients in this study.

Nevertheless in the era of minimally invasive medical procedures we believe that the concept of sentinel lymph node in colorectal cancer will gain its importance and find its place among the arsenal of clinical options for fighting this terrible disease.



## Scintigraphic evaluation of skeletal infections and inflammation with radiolabeled monoclonal antibodies: case report

Crcareva B<sup>1</sup>, Muratovska L<sup>1</sup>, Vaskova O<sup>2</sup>, Miladinova D<sup>2</sup>, Samardziski M<sup>3</sup>

<sup>1</sup>Clinical Hospital Acibadem-Sistina Skopje

<sup>2</sup>Institute of Pathophysiology and Nuclear Medicine, Medical Faculty Skopje

<sup>3</sup>Clinic for Orthopaedic Surgery, Medical Faculty Skopje

**Introduction:** Early and accurate diagnosis of skeletal infections and inflammations is still a challenge in routine nuclear medicine practice. Addressing this challenge are several established nuclear medicine procedures. Nevertheless the obtained results are not always translated in appropriate diagnostic outcome. Introducing the relative new radiopharmaceutical, radiolabeled monoclonal antibodies, is a great step forward in solving the problem of fast, accurate and reliable final diagnosis for patients suffering from this pathology.

**Aim:** To describe a case report of patient with osteomyelitis evaluated with morphological and functional imaging modalities.

**Case report:** A 56 years old female patient with suspected recidivated osteomyelitis on the right femur was scheduled for <sup>99m</sup>Tc MDP three phase bone scintigraphy. Previous laboratory examinations revealed high inflammation markers, also a suspected tumor formation or abscess in the middle distal diaphysis on the right femur, showing on a computed tomography scan (CT) and magnetic resonance imaging (MRI). A positive <sup>99m</sup>Tc MDP three phase bone scintigraphy indicated a bone metabolic reaction surrounding the primary lesion. Radiolabeled autologous leucocytes could not clearly differentiate presence of infection or osteomyelitis, but the radiolabeled monoclonal antibodies showed clear signs of osteomyelitis in the upper third of the femur as well as sterile inflammation in the middle distal diaphysis of the femur. Surgical intervention was performed. The patohystological report correlated with the findings obtained from the scintigraphy using radiolabeled monoclonal antibodies.

**Discussion:** Result obtained from different imaging modalities indicate that the radiolabeled monoclonal antibodies gave clearest visualization of the infection and also made a differentiation between the infection and the sterile inflammation.

## SENTINEL LYMPH NODE DETECTION IN MELANOMA MALIGNUM DORSI – CASE REPORT

**Authors:** Stojanoski Sinisa 1, Trencsev Viktor 2, Angjeleska Meri 1, Ristevska Nevena 1, Pop Gjorceva Daniela 1, Miladinova Daniela 1, Majstorov Venjamin 1, Ugrinska Ana 1, Vaskova Olivija1

**1** Institute of Pathophysiology and Nuclear Medicine, Acad “Isak S. Tadzer”, **2** Clinic for plastic and reconstructive surgery, Medical Faculty, Skopje

**Introduction:** Malignant melanoma is the most dangerous type of skin cancer. It develops from the pigment-containing cells known as melanocytes. Typically it occurs in the skin but may rarely occur in the mouth, intestines, or eye. In women it most commonly occurs on the legs, while in men on the back.

**Material and methodology:** We present a case of a 45 years old male patient diagnosed as malignant melanoma dorsi, with clinically negative lymph nodes. SLN detection was performed using gamma camera and gamma detection probe after subcutaneous peritumoral injection of (99m-Technetium-SENTISCINT). Blue dye was administered 20 min before the operation. SLNs were extirpated and histopathology was performed.

**Results:** SLN procedure, in the dynamic phase, presented triple drainage of the melanoma towards the both axillar regions, and one lymph drainage pathway towards the inguinal region. 3 lymph nodes were detected and surgically extirpated in the above mentioned regions. Histopathology was performed, and it presented all 3 extirpated lymph nodes positive.

**Conclusion:** Malignant melanomas of the back present unpredictable and multiple drainage patterns. In that manner, SLN detection technique is non invasive, safe, reliable and should be incorporated into the guidelines for malignant melanomas as a staging and therapeutic procedure.

## Prediction of histopathological type of synovial sarcoma by MRI; is it possible?

Violeta Vasilevska Nikodinovska<sup>1</sup>, Joan C Vilanova<sup>2</sup>, Filip Vanhoenacker<sup>3</sup>, Iris Noebauer-Hohmann<sup>4</sup>,

<sup>1</sup>University Surgical Clinic "St.Naum Ohridski" Skopje

<sup>2</sup>Clínica Girona, Girona

<sup>3</sup>University Hospital Antwerp, Edegem

<sup>4</sup>Clinic for Radiodiagnostic, Allgemeine Krankenhaus AKH, Viena

**Purpose:** To be presented magnetic resonance imaging (MRI) findings of synovial sarcoma, and to evaluate MRI parameters that predicts histopathological type of synovial sarcoma.

**Material and methods:** MRI of synovial sarcomas from four institutions was retrospectively analyzed. Out of 43 cases with synovial sarcoma, monophasic were 24 cases (56%), biphasic 17(39.5%) cases and two were low differentiated synovial sarcoma. 23 were males, and 20 females, with median age 40 years. Twenty four MRI parameters were evaluated. Multivariate logistic regression analysis, Mann-Whitney U test, Sperman rank order correlations, backward stepwise multiple regression analysis, standard multiple regression were used for imaging parameters predictive for differentiation of histopathology.

**Results:** Deep and extracompartmental localization has 79% of the cases. Most of the cases were with iso signal intensity (SI) in T1 and high and inhomogenous SI in T2, with peripheral (53%) and inhomogeneous (88%) enhancement. Cystic area and necrosis were equally present (53%). Mostly, hemorrhage and fluid-fluid level were absent. Multilocular configuration has 12(28%) cases. Sixty three percents of the cases were with well demarcated margins and in same percentage two different solid areas were present. Bone and joint involvement was rare.

Backward stepwise multiple regression analysis and standard multiple regression shows that no single MR parameter can be significant for prediction of histopathological type of synovial sarcoma.

**Conclusion:** None of evaluated MR parameter can't be independent predicting parameter for differentiation of histopathological types of synovial sarcoma.

## Clinical experience with TCm99MDP imaging in patients with malignant tumors-preliminary results

Veljanovska J, Mihajlovska S, Sekulovska M, Risteski Lj

Department of nuclear medicine ,Clinical hospital –Bitola

**Objectives** : Bone scintigraphy can uncover unique findings on its own as well as complement other imaging techniques. Also can provide a general indicator of malignant ,versus benign disease and may produce characteristic findings that are difficult to evaluate with other methods.

**Methods** :The study included 1433 patients (788 females and 644 males, aged 39-77 years) with histopatologically proven malignancy (Ca mammae, Ca recti, Ca pulmonum, Ca ventriculi, Ca uteri, Ca prostatae ) to detect malignant bone pathologies in period between January 2007 and December 2009. Bone scan was performed by the intravenous administration of technetium -99m methylene diphosphonate (Tcm99MDP) at a dose of 555-740 MBq .Images were asquired 3 hr after injection on a gamma camera scintigraphic protocol.(Mediso ,Hungaru)

**Results:** We retrospectively reviewed all patients biochemical and biopsy reports and patients were studied in each step. The computerization of the results showed higher number of patients with positive findings of the scan (66,8%) compared with normal bone scintigraphy ( 33,3%).As most common primary diagnosis in patients with bone metastases was represented Ca mammae 31,4% , Ca prostatae to 21,9% , and Ca pulmonum 23,4% .The most expressed accumulation of radiotracer Tcm99MDP is detected in the region of the spine 33,6%, pelvis bone of 26,7%, ribs (axial skeleton) 23,3% and less in lesion of long bones 16,2%.

**Conclusion:** Our preliminary clinical experience suggests that bone scan Tcm99MDP can be helpful in localizing malignant tumors ant that its sensitivity is slightly higher than other methods and also have good potential for the detection of malignant bone pathologies as well as assessing tumor response to therapy.

## **Daily Quality control for PET/CT**

**Bogojevska J, Muratovska L, Crcareva B, Stojanovska L, Anastasov G**

**1 Clinical hospital Acibadem-Sistina Skopje**

Introduction: Successful QC program will reduce artefact by reducing the likelihood of scanning with malfunctioning equipment. For PET/CT more important is the same general principles for any nuclear equipment with two factors: firstly the inclusion of CT, and secondly more quantitative nature of PET imaging. QC for PET scanner is the daily sinogram formed by irradiating the detectors uniformly with 511-keV photons from a long lived positron source or a  $^{68}\text{Ge}$  cylinder placed within the field of view. For every patient we have QC check, and we don't have good results if the QC is not measurement. Material and method. The fundamental requirement of the combined PET/CT data sets is that they are spatially aligned. The manufacturer will have procedures to separate gantries to a certain tolerance together to measure for any residual misalignment. We have cylinder  $^{68}\text{Ge}$  which is simple form for such a test. Discussion Daily and periodic QA test should follow the manufacturer recommendations, and without good QC there is not good results.

## **Detection of anti-thyroid peroxidase autoantibodies (antiTPO-Ab) in early diagnosis of autoimmune thyroid disease (AITD) by RIA assay**

**Mihajlova S, Sekulovska M, Risteski Lj, Veljanova K**

**Department of Nuclear Medicine, Clinical Hospital, Bitola**

This review will describe antiTPO-Ab in investigation of diagnosis Grave's and Hashimoto disease. These antibodies (particular antibodies against thyroid peroxidase) in thyroid autoimmunity were assayed by a sensitive and specific RIA method.

We evaluated the diagnostic validity of the anti-TPO assay in 222 patients with different types of thyroid autoimmune disease. The patients were divided in three groups: Group 1 - patients with Graves' disease (70), group 2 - patient with Hashimoto thyroiditis (91) and control group with 61 normal subjects. The study group included patients in different ages (28-67) and sex (176 female and 46 male) in the period from 2012- March 2015. The availability of an anti-TPO preparation allowed the development of sensitive radioimmunoassay technique.

The mean anti-TPO levels in control group was 25,76 IU/ml. The highest frequency positive results (100%) was obtained in patients with autoimmune hypothyroidism followed by patients with Graves' disease (51,4 %). Highly positive values of antiTPO-Ab were observed in autoimmune Hashimoto thyroiditis in median level of 1171,5 IU/ml. Serum concentration of anti-thyroid peroxidase were assayed in patient with Graves' disease in median level of 893,3 IU/ml. Anti-TPO Ab significantly decreased of over 27,8% ( $p < 0,05$ ) in patient with Graves disease after treatment with propylthiouracil. Treatment in autoimmune hypothyroidism showed median decrease of 10,65%.

Subjects with Hashimoto's thyroiditis and Graves' disease showed significant differences in level of anti-TPO-Ab compared with healthy donors. Anti-TPO Ab is an important marker, can be used as an early sign of thyroid function.

## ANTI-TPO CRUCIAL MARKER IN DIFFERENTIAL DIAGNOSIS IN THYROID AUTOIMMUNITY

Petrova Nasuh S<sup>1</sup> Kosturski N<sup>2</sup>

P.H.I Dr Kosturski – Biochemistry and Diagnostic Laboratory, Bitola

**Introduction**, Thyroid peroxidase (TPO) is present in thyroid cells microsomes having a key role in L-tyrosine iodization, a process essential for the formation of thyroid hormones. Anti-TPO antibody is a member of thyroid auto antibodies which are important in inducing and also diagnosing autoimmune thyroid diseases. Thyroid autoimmunity can cause several forms of thyroid dysfunction, ranging from hypothyroidism to hyperthyroidism. **Objectives**, Differential diagnosis between hypothyroidism and autoimmune thyroiditis.

**Methods**, During 2 year period, the concentrations of serum anti-TPO antibody (ELFA) , ATG and T3, T4, and TSH were measured. Screening procedures included a clinical examination, thyroid palpation, ultrasonographic examination.

**Results** 1375 subjects (age range between 18-75 years old) suspected of having thyroid disease referred to PHI Dr Kosturski laboratory. 257(18.7%) were male and 1118 (81,30%) were female. A correlation between TSH and high level of anti-TPO antibody was detected in 545 patients. Low TSH level and high T3/T4 levels was detected among 46 patients. High level of TSH and low levels of T3/T4 was found among 499 patients. Anti-TPO level was crucial in differentiating M. Basedow from Hashimoto thyroiditis.

**Conclusion**. Our results confirm the correlation between thyroid function test and anti-TPO antibody values, indicating the clinical significance of this antibody, suggesting a through clinical examination and follow up of individuals with high anti-TPO antibody titer.

## REMNANT ABLATION SUCCESS AMONG PATIENTS WITH DIFFERENTIATED THYROID CANCER

Laketić N, Kovačić K, Simić A

Special Hospital for Thyroid Gland and Metabolism Čigota, Zlatibor

*Introduction:* Department of Nuclear Medicine in our institution has started dealing with radioiodine therapy for differentiated thyroid cancer (DTC) in 2010. For the past 5 years we have treated 596 patients in existing two rooms of the therapeutic section. We are in the procedure for increasing capacity with two more rooms and this process will be finished by September 2015.

*Objectives:* The aim of this work is to evaluate remnant ablation success among patients with DTC who have been treated with I-131 in Čigota Special Hospital.

*Methods:* Patients included in this study received ablation dose (No/Nx and Mo/Mx stage of disease) of radioiodine in Čigota Special Hospital. Follow up of these patients was conducted in our institution. Criteria for defining success of remnant ablation were negative whole body scan (WBS) 12+ months after ablation therapy as well as negative tumor markers (thyroglobulin and anti-thyroglobulin antibodies) under elevated TSH (>30 mIU/l) stimulation. At final, our results were compared with the results from the studies of other Departments dealing with DTC.

*Results:* Thirty seven patients (78.7%) had negative WBS and markers. Nine patients (19.1%) needed reapplication and one patient (2.2%) had negative WBS and positive markers and was sent to PET/CT.

*Conclusion:* Results of other ablation success studies vary between 43% and 87.6%. Our results are positioned in expected range. Success of remnant ablation is also in correlation with successful surgery.



## LONG TERM THYROID FUNCTION AFTER J – 131 TREATMENT OF TOXIC THYROID ADENOMA

Z.Petrovski, K.Trajkovska, J.Gjorgievski

Department of Nuclear Medicine, Clinical Hospital, Bitola

**Objective:** The aim of the study was to analyze the outcome of J- 131 therapy for autonomous thyroid adenomas in long period of follow up.

**Material and Methods:** We estimated 68 pts with Plummer's disease ( 50 females, 18 males, mean age 54,7 yrs, range 21 – 79 yrs) for period 1995 – 2014. 92.6%(63/68) pts had a unifocal nodule, while 7.4% (5/68) pts had multifocal toxic autonomous nodules.Pts stopped antithyroid drugs for at least one month prior to the radioiodine treatment and than we administered a J- 131 activity of 740 -+200 MBq (range 550 – 1100 MBq), based of size and weight of “hot” nodules and the value of radioiodine uptake.Volumetry was done by ultrasound.The mean duration of follow up was 5,84 years.

**Results:** In 65/68 (95%) pts was administered a single dose, while 3/68 (5%) pts needed two doses. 55/68 (80.9%) pts who treated with radioiodine were euthyroid with scintigraphic normalization.The percentage of euthyroid did not significantly change in long term of 20 years observation. The recurrent hyperthyroidism was 2,9% (2/68) pts.The cumulative incidence of hypothyroidism was 16.2% (11/68) pts withing 1 – 6,2 yrs.Hypothyroidism developed earlier in patients who were euthyroid before J-131 therapy (3,5 – 7,7 months) than in the subclinically hyperthyroid patients, who became hypothyroid within 7,2 – 13,6 months ( $p=0.001$ ). The development of hypothyroidism was higher in pts who showed extranodular uptake and after TSH suppression The nodular volume was statistically higher in pts who had recurrent hyperthyroidism over hypothyroidism ( $p<0,01$ ) and euthyroidism ( $p<0,02$ ).No differences were observed in the results between unifocal and multifocal nodules.

**Conclusion:**J – 131 therapy is a simple, safe and effective treatment of autonomous functioning thyroid adenoma with a low rate of recurrent hyperthyroidism (3%) and development of hypothyroidism (16%).

## **THYROIDITIS AND URTICARIA CAUSED BY HELICOBACTER PYLORI**

**Antigona Begolli Gerqari(1), Idriz Gerqar(2), Mybera Ferizi(1), Sadije Halim(1), Aferdita Daka(1), Syzana Hapciu(1), Mirije Begolli(3), Ilir Begolli(4)**

**1. Dermatology Clinic-University Clinical Center Prishtina**

**2. Department of Nuclear Medicine-University Clinical Center Prishtina**

**3. Pediatric Clinic-University Clinical Center Prishtina**

**4. Institute of Public Health –Prishtina**

**INTRODUCTION:**Helicobacter pylori is gram negative bacteria resident in the stomach but it can also invade other organs . In addition, there is also proof that helicobacter pylori can cause skin problems, in most cases urticaria .

**OBJECTIVES:**The aim of this work was to document that helicobacter pylori is one of the major causes often undermined for causing acute thyroiditis and urticaria.

**CASE REPORT:**We present the case of a 53 year old man with a history of a chronic gastritis and a sudden upset of the throat pain, especially in palpation, problems with swallowing and skin rash diagnosed all of which concluded that the patient was struck with acute urticaria.

**RESULTS:**The analysis showed elevated sedimentation of erythrocytes, leukocytosis and neutrophilia; furthermore, the data also revealed that the patient had high levels of T3 and T4 and a lower level of TSH; helicobacter pylorus was also found in his feaces analysis. We applied the triple therapy against helicobacter pylori, and during the first week corticosteroids . The patient revealed signs of improvement . The symptoms disappeared entirely after two weeks of treatment .

**CONCLUSION:**Helicobacter pylori is one of the most common and most undermined causes of thyroiditis and urticaria.

## **HYPERTHYROSIS AND PSORIASIS VULGARIS**

**Sadije Halimi(1),Mybera Ferizi(1),Antigona Gerqari(1),Idriz Gerqari(2),Mirije Begolli(3),Ilir Begolli(4)**

**1.Dermatology Clinic-University Clinical Center Prishtina**

**2.Nuclear Medicine Department-University Clinical Center Prishtina**

**3.Pediatric Clinic-University Clinical Center Prishtina**

**4.Institute of Public Health-Prishtina**

**INTRODUCTION:** Hyperthyroidism is an autoimmune disease that can be accompanied with other autoimmune disease. Hyperthyroidism can have implications on the skin. There are known cases where psoriasis vulgaris is a follower of hyperthyroidism as well as other thyroid gland disease.

**CASE REPORT:** We present the case of a 60 year old woman with a long history of psoriasis vulgaris. A few weeks before the patient showed signs of worsening of these symptoms, was referred to our clinic for further examination. The patient also complained of the hyperhidrosis, swelling of the arms and feets, palpitations, and high blood pressure.

**RESULTS:** We took a blood sample and the analysis showed only problems with thyroid gland. There were increased levels of T3 and T3, and depression of TSH. The scintigraphy of the thyroid gland showed hot nodule in a left thyroid gland. The same results came from the ultrasonography of the thyroid gland.

**CONCLUSION:** The autoimmune disease of the thyroid gland can be associated with other autoimmune diseases. It is very common to be associated with a skin autoimmune disease. Psoriasis vulgaris can follow all autoimmune disease of thyroid gland including hyperthyroidism as well as hypothyroidism.

**PAPILLARY THYROID CARCINOMA IN OVARIAN TERATOMA - case report**  
**Pop Gjorcheva D<sup>1</sup>, Vaskova O<sup>1</sup>, Ristevska N<sup>1</sup>, Stojanoski S<sup>1</sup>, Stojcevski S<sup>2</sup>**  
**Institute of Pathophysiology and Nuclear medicine "Academic Isak S. Tadzer"<sup>1</sup>, University Clinic of gynecology and opstetrition<sup>2</sup>, Medical Faculty, University "Ss.Cyril and Methodius", Skopje**

***Introduction:***

Papillary thyroid carcinoma (PTC) in ovarian teratoma is an extremely rare condition with certain difficulties in preoperative diagnosis and challenges in postoperative treatment strategy. Being either asymptomatic (and detected incidentally) or with nonspecific clinical symptoms, it should be promptly refer to an oncologist for surgical management of the possible malignancy.

***Case report:***

A 26 year-old women, mother of two children, recently diagnosed with breast fibroadenoma (BIRADS 4), preoperatively underwent pelvic ultrasonography, which revealed a presence of a large ovarian tumor (9cm) on the left side. Laparoscopic ovarian cystectomy was performed along with fibroadenomectomy. Pathohistology confirmed a diagnosis of PTC in ovarian teratoma. The thyroid examinations showed euthyroid condition of the patient, with normal thyroid and neck morphology (by ultrasonography) and normal thyroglobulin (Tg) value. The PET-CT scan showed no sites of metastatic spread from the primary cancer. The patient was informed about the postoperative treatment approaches (surgical, oncological and nuclear medicine protocols). Until the patient's final decision, suppressive doses of levothyroxine (150 microg/day) were advised.

***Conclusion:***

Currently, no consensus exists on the surgical and postoperative treatment of those patients. The therapy ranged from radical surgery (hysterectomy and bilateral salpingo-oophorectomy) and radio-chemotherapy, followed by thyroidectomy and I-131/ Tg postoperative PTC management protocols, to conservative surgery in younger patients with preservation of fertility.

## **Minimal Invasive Thyroidectomy (MIT) in surgical treatment of thyroid disease**

**Smilevski D, Muratovska L, Karagjozov M, Crcareva B, Jashar Dz, Kubelka K, Filipovski V**

**Clinical Hospital Acibadem Sistina, Skopje**

### **Abstract**

Postoperative aesthetic result in surgery of the thyroid gland is one of the most important aspects in these patients, especially women. Because of this, reduction in the length of the cervical incision is of particular interest in this group of patients. Recent years have demonstrated more minimally invasive surgical techniques for diseases of the thyroid and parathyroid glands, with the primary goal of a better cosmetic effect. But, the concept of surgical invasiveness cannot be limited only to the length of the skin incision, but must refer to other structures dissected during the procedure. So minimally invasive thyroidectomy should be defined as a surgical technique conducted through a small incision in the skin (less than 4cm), which provides direct access to the thyroid result in focused dissection. The type of anesthesia, duration of surgery, postoperative pain, possible complications and the rate of success and long-term therapeutic outcome, should be taken into account.

Minimally invazive thyroidectomy minimize the trauma of surgery not only in terms of the length of the skin incision, but also allows a better and direct access to the thyroid lodge, less extensive dissection, minimizes postoperative pain and gives a better aesthetic result.

## Increased incidence of positive thyroid antibodies in women with repeated unsuccessful cycles of in vitro fertilization

Muratovska L 1, Miladinova D 2, Crcareva B 1, Cokrevska Zografska N 1, Lazarevski S 1

1 Clinical Hospital Acibadem Sistina, Skopje, R Macedonia

2 Institute of Pathophysiology and Nuclear Medicine, Medical Faculty Skopje

**Introduction:** Autoimmune thyroid diseases are very common in women of reproductive period. They are characterized by the presence of anti-thyreoglobulin (aTG) and anti-thyreoperoxidase (aTPO) antibodies known as anti-thyroid antibodies (ATA). ATA are found in subjects with hypo- or hyperthyroidism, but also they are rarely found in patients without any sign of thyroid dysfunction. Analysis of previous studies indicates that infertility with female factors often include thyroid autoimmunity. Even women without any signs of thyroid dysfunction, which were ATA positive (ATA +) are three to five times in higher risk of miscarriage than negative ATA (ATA -) women. ATA positivity can be associated with adverse pregnancy and birth in the procedures of in vitro fertilization (IVF). But other studies have failed to detect any difference in the success rate of IVF between ATA+ and ATA- women.

**Motives and objectives:** The motive for this study was to show the incidence of anti-thyroid antibodies in euthyreotic and women with subclinical hypothyreosis, who had one or more previous failed IVF cycles. The aim is to confirm or reject the need for routine screening of ATA before IVF.

**Material and Methods:** The study was conducted at the Department of Nuclear Medicine and the Department of assisted reproduction at the Clinical Hospital Acibadem Sistina in Skopje.

Examined were serum ATA (aTG and aTPO), FT3 and TSH in 60 patients (30 euthyroid and 30 with subclinical hypothyreosis), aged from 23 to 41 y., with different reasons for infertility, who had earlier confirmed one or more failed IVF cycles, and no previous births, proven thyroid disorder or other autoimmune diseases. Analysis of ATA were performed in the clinical biochemistry laboratory in Clinical Hospital Acibadem Sistina on apparatus COBAS e 411 from ROCHE Diagnostica, that is automated, computerized analyzer for immunological tests based on method ElectroHemiLuminescency.

**Results:** From total 60p. (30 euthyroid, 30 with subclinical hypothyreosis), 32p.(53%) are + for both ATA, 28p. (47%) are ATA-. 7p.(22%) are only aTPO+, 6p.(19%) only aTG+ and 19p.(59%) + for both ATA. From euthyroid group of patients 14 of 30p. (46%) showed a positive both ATA, 4p.(28%) are only aTPO+, 4p. (28%) are only aTG+, and 6p. (44%) are positive for both antibodies. 16 from

30p. (54%) are ATA -. From group of patients with subclinical hypothyreosis 18 of 30p. (60%) showed a positive titer of both ATA, 3p.(17%) are only aTPO+, 2p (11%) are only aTG+, and 13p.(72%) are positive on both antibodies. 12 from 30p. are ATA-.

ATA% after failed IVF procedure, in our study is 53% out of all patients, and that % is higher in patients with subclinical hypothyreosis (60%). We did not found high incidence of ATA in euthyroid women with history of one or more failed IVF cycles.

Futher investigations are needed to take into account other factors and to confirm the need for routine ATA screening in patients before IVF procedures.

## **Thyroid incidentaloma detected by F-18 FDG PET/CT: case report**

**Muratovska L, Crcareva B, Anaastasov Gj, Bogojevska J, Stojanovska L**  
**Clinical Hospital Acibadem Sistina, Skopje**

**Introduction:** Thyroid incidentalomas are fairly common and are actually previously undiagnosed thyroid lesions detected by tests conducted for other purpose, such as methods for cancer screening. Such lesions are often detected in patients who undergo FDG-PET/CT scan for another reason. In recent years FDG PET/CT scans as part of cancer screening has become more popular. It has also become more frequent method for detecting incidental thyroid lesions. Thyroid incidentalomas detected by FDG PET/CT scan have been reported in 1% to 4% of the population, with the risk of malignancy from 27.8% to 74%. On PET scans, incidentalomas are displayed as focal FDG accumulation, as opposed to diffuse accumulation in cases of thyroiditis. In routine thyroid practice, is still not recommended the use of PET scans to determine whether a thyroid nodule is benign or malignant. Fine-needle aspiration biopsy (FNAB) remains the method of choice for the diagnosis of the nature of thyroid nodules. Significance of FDG-PET/CT scanning in detecting thyroid incidentalomas remains unclear.

**Objective:** To show the case of thyroid incidentaloma with high FDG accumulation detected by FDG-PET / CT scan, which is made for screening in patients with other type of cancer.

**Case report:** A 66-year-old female patients, with previous results of biopsy of right axillary lymph nodes that confirmed metastases from malignant epithelial neoplasm, underwent FDG-PET/CT scan in our department for detection of localization of primary cancer site. FDG –PET/CT detected pathological FDG accumulation in right breast and rectum as a site of primary cancer, but also it detected a focal FDG accumulation (with SUV 6.4) in lower half of right thyroid lobe. Ultrasonography show unchomogenous node of 30mm. with calcifications and small cystic degenerations in the right thyroid lobe. FNAB of the node was suspected for papillary carcinoma, but metastatic lesion could not be ruled out. The patient underwent surgery, a total thyroidectomy, which passed without complications. Final pathohystology findings confirmed papillary carcinoma in the right lobe of the thyroid gland. Radioiodine therapy followed.

**Discussion:** Accidentally discovered lesions in the thyroid gland using FDG-PET/CT scans are common. The use of FDG-PET/CT scanning to screen for thyroid incidentalomas in healthy individuals is questionable. For individuals whose thyroid incidentalomas are detected during FDG-PET/CT scan as part of



the cancer screening program, there is a high risk of malignancy. Also, the results of this case suggest that the focal thyroid FDG accumulation and high SUV have high risk for thyroid malignancy in thyroid lesion incidentally found and we need further investigation such ultrasonography and FNAB, followed by possible surgery. When cytological results are unsatisfactory, FDG-PET/CT scan may be useful method for differentiating benign from malignant thyroid nodes. We need further studies on this subject, but FDG-PET/CT scan can play a role in the evaluation of thyroid incidentalomas detected during regular cancer screening.

## CHARACTERISTICS OF BREAST CANCER PATIENTS REFERRED FOR BONE SCAN

Ismaili I<sup>1</sup>, Ugrinska A<sup>2</sup>, Vasev N<sup>1</sup>, Peseva M<sup>1</sup>, Bozinowska N<sup>2</sup>, Pajenga E, Tripunoski T<sup>2</sup>, Miladinova D<sup>2</sup>

University Clinic of Radiotherapy and Oncology, Medical Faculty, UKIM, Skopje<sup>1</sup>

Institute of Pathophysiology and Nuclear Medicine "A. Isak S. Tadzer", Medical Faculty, UKIM, Skopje<sup>2</sup>

Department of Biology, Faculty of Natural Science, University of Elbasan, Elbasan<sup>3</sup>

Bone scan is the most commonly used method in the evaluation of breast cancer patients for skeletal metastases. Although there are controversies the most frequently used algorithm is that this procedure is omitted in patients at early stage of the disease at initial staging, and used only in patients with advanced disease. During the follow-up usually it is used when patients develop skeletal related symptoms.

**Aim:** The aim of this study is to investigate the characteristics of breast cancer patients referred for bone scan with findings positive for bone metastases in regard to the TNM, pathohistology, estrogen and progesterone receptor status.

**Material and method:** Retrospective analysis was performed of the files of 87 patients from the University Clinic for Radiotherapy and Oncology in Skopje that were referred for bone scan at the Institute of Pathophysiology and Nuclear Medicine in Skopje. Data for bone scan findings, TNM, pathohistology, estrogen and progesterone receptor status were analyzed.

**Results:** From the referred patients 32% had bone scan findings indicative for metastases. Out of this number 75% had ductal type of carcinoma. In regard to the TNM, 68% were N positive, 49% 18% had T1, 50% T2 and the rest of them had T3 and 4. There was only one patient with known distant metastases. Regarding the estrogen receptor status all patients except one showed positive findings, 75% were progesterone receptor positive and only one patient was triple negative.

**Conclusion:** Patients with positive bone scan findings were more likely to have nodal involvement and estrogen receptor positive findings. In regard to tumor size our results showed that only 18% patients had small tumors, and the rest of them were in T stages 2-4.



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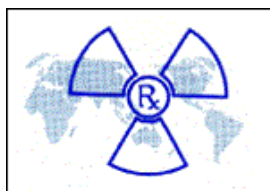
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